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Reactions related to the pinacol-pinacone rearrangement. Part II. The fate of the carbonium ion derived from 2-methylpropane-1 : 2-diol. By J. B. Ley and C. A. Vernon

XUM

373. *Vapour Pressures of Mixtures of Dinitrogen Tetroxide with Donor and with Non-donor Organic Solvents : Comparison with Some Nitrosyl Chloride Systems.*

By C. C. Addison and J. C. Sheldon.

Vapour pressures are recorded for mixtures of dinitrogen tetroxide with the following solvents over the full concentration range at 0° : carbon tetrachloride, chlorobenzene, benzene, toluene, nitrobenzene, benzyl cyanide, methyl cyanide, and acetic acid. Vapour pressures of mixtures with *n*-heptane, chloroform, nitromethane, acetic anhydride, and ethyl acetate are recorded from −10° to +10°, and a few measurements are reported for mixtures with *cyclo*hexane, dioxan, and diethylnitrosamine. Deviations from ideal behaviour are correlated with the polar nature and donor properties of the solvents, and the degree of addition-compound formation in the liquid. For comparison, vapour pressures of mixtures of nitrosyl chloride with chloroform, pyridine, and ethyl acetate have been measured over the range −50° to −20°.

Liquid dinitrogen tetroxide, when used as a reactant, is frequently diluted with organic solvents. Previous papers [1] have illustrated the wide range of organic compounds capable of forming addition compounds in the solid state, and addition compounds are present in the liquid mixtures also. In some reactions the presence of the tetroxide–solvent complex may not influence the course of a reaction; Sisler and his co-workers, studying compound formation between heterocylic amines and dinitrogen tetroxide in ether, found the dissociation of the ether–tetroxide complex to be so far advanced above its melting point that the amine–tetroxide reaction was not affected.[2] In contrast, propene and the butenes with liquid dinitrogen tetroxide give oxidation products which contain little or no nitroparaffin, whereas in a 50% (w/w) solution of the tetroxide in diethyl ether, oxidations are almost entirely prevented.[3] Again, nitration of the benzene ring by dinitrogen tetroxide is promoted by addition of acetic anhydride.[4] Our study of the molecular addition compounds has therefore been extended to the liquid state, which is represented by the equilibrium

$$\underset{(A)}{[(\mathrm{Don})_n\mathrm{NO}^+]\mathrm{NO}_3^-} \rightleftharpoons n(\mathrm{Don}) + \mathrm{N_2O_4} \rightleftharpoons \underset{(B)}{(\mathrm{Don})_n\mathrm{N_2O_4}}$$

(Don) is the donor solvent; the small proportion of complex (*A*) influences profoundly the reaction of the mixtures with metals.[5] The value of *n* cannot be determined in the liquid as readily as in the solid, but with weak donor solvents it is unlikely that *n* differs from unity. The presence of molecular addition complexes (*B*) is not usually obvious in the liquid, since in rare cases only (*e.g.*, with dimethyl sulphoxide,[1a] 1 : 4-dioxan,[3b, 6] and ethyl phenylpropiolate [7]) does an addition compound crystallise on mixing solvent and tetroxide at room temperature. The colours which some mixtures develop indicate electron transfer,[1a, 1c] but in general such electron transfer provides only an additional (and not necessarily the predominant) type of molecular attraction, so that its influence on the physical properties of tetroxide mixtures cannot be deduced from measurements with any one solvent; a range of solvents having differing structure and polar character has therefore been employed.

[1] Addison and Sheldon, *J.*, 1956, (*a*) 1941, (*b*) 2705, (*c*) 2709.
[2] Davenport, Burkhardt, and Sisler, *J. Amer. Chem. Soc.*, 1953, **75**, 4175.
[3] Levy and Scaife, *J.*, 1946, (*a*) 1093, (*b*) 1096, (*c*) 1100.
[4] Valynashko, Bliznyukov, and Lutskii, *Trudy Khar'kov Khim.—Tekhnol. Inst. im S.M. Kirova*, 1944, *No.* 4, 48 (*Chem. Abs.*, 1948, **42**, 1218 f).
[5] Addison, Sheldon, and Hodge, *J.*, 1956, 3900.
[6] Rubin, Sisler, and Shechter, *J. Amer. Chem. Soc.*, 1952, **74**, 877.
[7] Wieland, Schamberg, and Wagner, *Ber.*, 1920, **53**, 1343; Wieland and Blümich, *Annalen*, 1921, **424**, 100.

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Because of the high volatility of dinitrogen tetroxide compared with that of the solvents used, the vapour pressure of the mixtures reflects the behaviour of the tetroxide in the liquid, and can be interpreted in terms of the degree of association between dinitrogen tetroxide and the organic component. Comparison of the deviations from Raoult's law for a range of solvents provides a measure of the relative significance of the various types of molecular interaction occurring in the mixtures. The theory of the liquid state is not sufficiently developed to permit quantitative assessment of the separate interactions when the components possess one or more polar, donor, or acceptor groups, so that the deductions are at present largely qualitative. There are clear correlations between vapour pressure, heats of mixing, and dipolar character of the solvent which will be discussed in a later paper.[8]

Results and Discussion

The vapour pressures of mixtures with the organic compounds listed in Table 1 are given in Figs. 1—3. The compounds are arranged in order of percentage deviation, which is defined as $100(P_{observed} - P_{ideal})/P_{ideal}$, for equimolecular mixtures, P_{ideal} being the vapour pressure which the system would possess if Raoult's law were obeyed. Vapour pressures

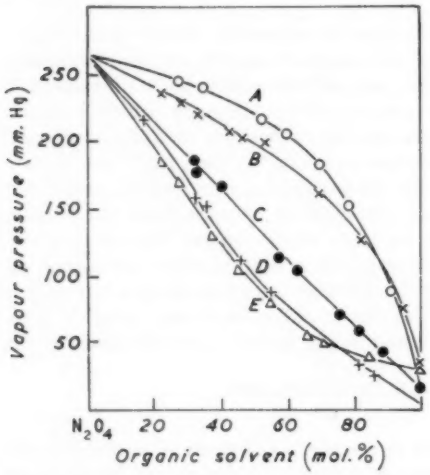

Fig. 1. *Vapour pressures of* N_2O_4 *organic solvent mixtures at 0°.*

A, *n*-Heptane; *B*, carbon tetrachloride; *C*, nitromethane; *D*, acetic anhydride; *E*, ethyl acetate.

for all thirteen systems in Figs. 1—3 have been measured at 0° and for five systems (Table 2) measurements are recorded over a range of temperature.

Tables 1 and 2 and Figs. 1—3 show that by varying the organic component it is possible to obtain vapour-pressure systems covering the full range from strongly positive, through zero, to strongly negative deviations. Compounds marked by an asterisk in Table 1 are known to form addition compounds with dinitrogen tetroxide in the solid state.

Vapour-pressure data for three systems, which have not been fully examined, are given in Table 3. The results for diethylnitrosamine indicate a deviation of approximately −30%, which supports previous evidence [8a] of well-developed compound formation in the liquid state. Crystallisation of the addition compound from dioxan–tetroxide mixtures [6] restricted the concentration range available, and the melting point of dioxan (11·7°) limited the temperature range for this system. No firm estimate of the percentage deviation at the equimolecular point can therefore be made for comparison with the values in Table 1, but the deviations from P_{ideal} for dioxan-rich mixtures are as large as for other oxygen donors (*e.g.*, ethyl acetate) at similar concentrations.

[8] Addison, Sheldon, and Smith, *J.*, 1957, in the press.
[8a] Addison and Conduit, *J.*, 1952, 1390.

TABLE 1.

Organic component	Deviation at 0° (%)	Dipole moment of organic component (D)	Fig. No.
n-Heptane	55·5	0	1 (Table 2)
Carbon tetrachloride	33	0	1 (Table 2)
Chloroform	21	1·15	2
Chlorobenzene	18·5	1·56	3
*Benzene	9·5	0	3
Toluene	6	0·39	2
Nitromethane	0	3·17	1 (Table 2)
*Nitrobenzene	− 6	3·99	3
*Benzyl cyanide	−15·5	3·50	2
*Methyl cyanide	−16	3·37	2
*Acetic anhydride	−28	2·80	1 (Table 2)
*Acetic acid	−34	0·83 [a] 1·75 [b]	3
*Ethyl acetate	−34	1·81	1 (Table 2)

[a] Dimer. [b] Monomer (Potapenko and Wheeler, *Rev. Mod. Phys.*, 1948, **20**, 143; Pohl, Hobbs, and Gross, *Ann. New York Acad. Sci.*, 1940, **40**, 389).

TABLE 2. *Vapour pressures (mm.) of N_2O_4–organic solvent mixtures at various temperatures.*

Temp.								
n-C_7H_{16} (mol %)	0	25·0	33·5	51·8	59·5	69·5	76·5	91·4	100
10°	444	400	392	340	322	280	228	138	20
5	343	315	307	270	358	228	185	112	15
− 5	201	187	185	169	160	142	120	70	9
−10	151	143	140	129	125	112	93	54	7
CCl_4 (mol. %)	22·7	28·6	33·2	43·2	53·0	70·0	82·4	95·0	100
10	390	377	366	345	322	264	207	122	56
5	305	296	285	270	252	205	160	95	43
− 5	180	174	162	160	151	127	97	55	25
−10	136	132	128	123	116	98	74	42	18
$Me{\cdot}NO_2$ (mol. %)	21·6	31·4	39·5	56·5	62·2	75·5	81·0	88·0	100
10	348	313	280	200	179	120	103	77	16
5	269	241	214	153	136	93	77	56	11
− 5	155	137	123	85	75	50	42	31	6
−10	118	104	92	63	55	37	31	23	4
$(Me{\cdot}CO)_2O$ (mol. %)		17·2	30·8	35·0	45·0	54·2	81·5	85·0	100
10		355	270	242	183	145	60	50	<3
−10		117	87	81	62	49	19	16	~0
−20		60	47	43	32	27	12	10	~0
$Me{\cdot}CO_2Et$ (mol. %)	22·8	28·0	37·6	44·5	55·2	67·0	70·6	84·0	100
10	312	287	226	197	148	104	92	70	43
5	241	225	168	146	111	78	70	53	33
− 5	137	126	96	84	62	43	39	29	18
−10	103	92	73	62	45	31	28	21	13

TABLE 3.

Compn. of mixture (mol. % of solvent)	Vapour pressure (mm.) at −10°	0°	10°	15°	20°
Diethylnitrosamine					
0·0	151	263	444	564	720 [a]
31	89	160	—	—	—
56	36	66·5	120·5	—	—
72	14·5	29	55*	—	—
100	~0	~0	~0	—	—
*cyclo*Hexane					
58	124·5	207	325		
100	—	—	48·5		

Compn. of mixture (mol. % of solvent)	Vapour pressure (mm.) at 10°	15°	20°
1 : 4-Dioxan			
7·0	409	523	650
8·1	401	511·5	633
89·6	32·5	44	57
90·5	32·5	44	55·5
95·7	24	32·5	43
96·5	24	32	41·5
100	—	21·5	27

[a] Giauque and Kemp, *J. Chem. Phys.*, 1938, **6**, 40.

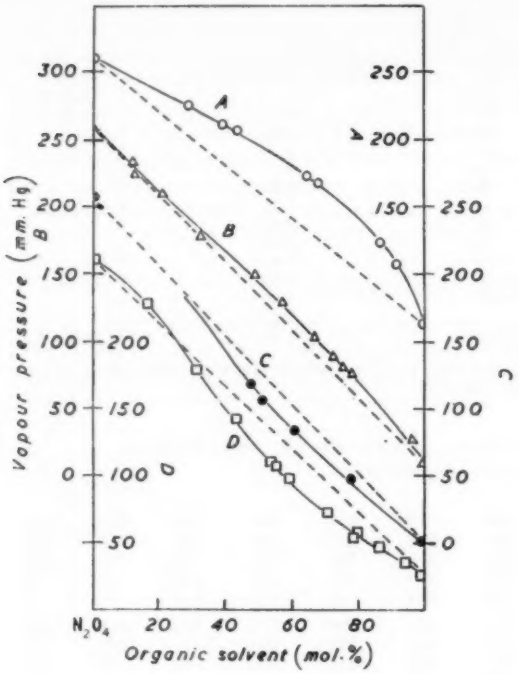

FIG. 2. *Vapour pressures (mm.) of N_2O_4–solvent mixtures.*

N_2O_4 with: *A*, chloroform; *B*, toluene; *C*, benzyl cyanide; *D*, methyl cyanide.

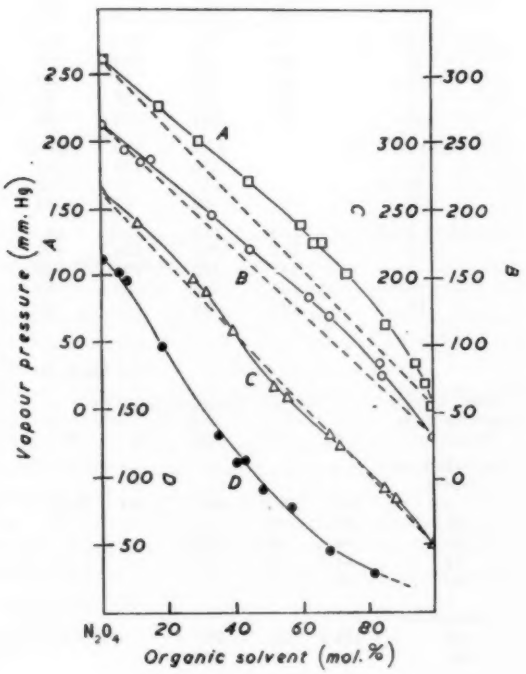

FIG. 3. *Vapour pressures (mm.) of N_2O_4–solvent mixtures.*

N_2O_4 with: *A*, chlorobenzene; *B*, benzene; *C*, nitrobenzene; *D*, acetic acid.

Vapour Pressure of Non-donor Solvent–Dinitrogen Tetroxide Systems.—The *n*-heptane system shows the largest positive deviation observed in dinitrogen tetroxide systems, and probably represents a limiting case. Any attraction between the two molecules involves dispersion and induction effects, and in this instance is clearly small. The behaviour of the *cyclo*paraffins is similar to that of the straight-chain hydrocarbons (cf. *cyclo*hexane, Table 3). Carbon tetrachloride, chloroform,[9] and nitromethane are also non-donors; the positive deviation diminishes with increase in dipole moment (Table 1), indicating increasing molecular attraction by dipole interaction. Carbon tetrachloride has no dipole moment but can be considered as having polar character, since the carbon–chlorine bond is dipolar.

Autocomplex-formation in Dinitrogen Tetroxide.—In the tetroxide molecule the two polar nitro-groups are opposed, giving a non-polar molecule. However, as observed above for carbon tetrachloride, the cancellation of identical opposed dipoles is not completely effective at distances of the order of molecular dimensions, and some dipole attraction probably exists between tetroxide molecules. It is suggested that some electron-exchange forces also exist in the pure liquid tetroxide; the " autocomplexes " so formed resemble the benzene–benzene autocomplexes postulated by Mulliken,[10] in which it is assumed that some π–π bonding exists between the aromatic molecules. Whereas mixtures of saturated hydrocarbons behave almost ideally (the *n*-heptane–*n*-hexane system gives an almost zero vapour-pressure deviation [11] at 30°), systems containing benzene show pronounced positive deviations (the *n*-heptane–benzene and *cyclo*hexane–benzene systems give deviations of +10·4% at 80° [12] and +12·2% at 40° [13] respectively). There is a general similarity in the spacial distribution of the π orbitals of benzene and dinitrogen tetroxide, and some π–π bonding between tetroxide molecules could also readily account for the positive deviations shown by its mixtures with saturated hydrocarbons.

Aromatic Hydrocarbon Systems.—Measurements have been restricted to benzene and toluene, since other aromatic hydrocarbons were too rapidly attacked by the tetroxide. These two compounds give much smaller positive deviations than does carbon tetrachloride or chloroform; this alone indicates some form of aromatic hydrocarbon–dinitrogen tetroxide bonding other than those of dispersion, orientation, or induction. Thermal analysis shows that aromatic hydrocarbons are π donors with respect to the tetroxide,[1a] and this is sufficient to reduce the deviation from 55·5% for a paraffin to 9·5% for benzene. Since the deviation is still positive, the aromatic hydrocarbon–tetroxide bonding is weaker than the sum of polar and π–π bonding between tetroxide molecules.

Aliphatic 'Onium Donor Systems.—Methyl cyanide (an 'onium donor) and nitromethane have similar dipole moments (Table 1) and their dipole interaction with dinitrogen tetroxide should be similar in the two cases. The deviation of −16% for methyl cyanide demonstrates the presence of compound formation in the liquid mixture. However, when the deviations for methyl cyanide and nitromethane are compared with the limiting deviation given by *n*-heptane, it is seen that the proportion of the deviation change which can be ascribed to compound formation with methyl cyanide is much smaller than that to be attributed to polar association. The larger negative deviations observed for the oxygen donors acetic anhydride and ethyl acetate indicate a greater degree of compound formation, but for all the 'onium donor solvents examined here compound formation involving the tetroxide molecule as an electron acceptor makes a smaller contribution to molecular association than does dipole–dipole interaction.

The Acetic Acid System.—Frankland and Farmer [14] have shown from ebullioscopic measurements that some carboxylic acids are dimerised in solution in dinitrogen tetroxide,

[9] Musil and Breitenhuber, *Z. Electrochem.*, 1953, **57**, 423.
[10] Mulliken, *J. Amer. Chem. Soc.*, 1952, **74**, 811.
[11] Smyth and Engel, *ibid.*, 1929, **51**, 2646.
[12] Brown, *Austral. J. Res.*, 1952, *A*, **5**, 530.
[13] Scatchard, Wood, and Mochel, *J. Phys. Chem.*, 1939, **43**, 119.
[14] Frankland and Farmer, *J.*, 1901, **79**, 1356.

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and this is now shown to be true for acetic acid. The dinitrogen tetroxide–acetic acid phase diagram,[1a] when plotted with respect to molecular percentage of acetic acid, gives an N_2O_4-rich liquidus curve having smaller slope than corresponding curves for acetic anhydride or ethyl acetate. When composition is plotted as mol. % of the acetic anhydride dimer, the liquidus curve comes into close agreement. Because the acid has m. p. 16°, the full vapour-pressure curve at 0° is not available, and percentage deviations can only be estimated. When vapour pressure is plotted against mol. % of monomer, a slight positive deviation results, which is not in accord with similar systems. Plotted in terms of mol. % of dimer, the deviation is approximately −34%, which is near that for similar oxygen donors.

Systems containing Aromatic Hydrocarbon Derivatives.—Chlorobenzene forms no solid compound with dinitrogen tetroxide,[1a] but this may be a steric effect and does not preclude consideration of electron exchange in the liquid state as contributing to molecular association. However, the chlorobenzene deviation is appreciably greater than that for benzene; it is slightly less (and the dipole moment slightly greater) than for chloroform, indicating that polar association is the only major interaction between chlorobenzene and dinitrogen tetroxide, π bonding being insignificant. This is consistent with the well known deactivating effect which a substituted chlorine atom has on an aromatic nucleus. (Compare also the influence of the chlorine atom on ether–dinitrogen tetroxide compound formation.[1a])

The deviations for nitrobenzene and benzyl cyanide are similar to those for their aliphatic relatives nitromethane and methyl cyanide. It appears to be a general rule that when an aromatic compound has a near-zero dipole moment, π–π bonding can make a significant contribution to molecular association in the liquid, but that when the aromatic compound has a large dipole moment, the properties of the liquid are determined much more by polar association than by π–π bonding.

Inflexions in Vapour-pressure Curves.—The curves for nitrobenzene, methyl cyanide, and (to a less extent) nitromethane show one or more inflexions, an unusual feature in vapour-pressure studies. The forces which make up the total molecular attraction will depend in different ways on the molecular structure and molecular arrangements of the components in the liquid. Not all these forces will vary similarly with intermolecular distance and thus with relative concentration of the components. Results indicate that such variation in these forces with concentration is small compared with their total magnitude; they are not readily apparent when super-imposed on curves showing pronounced positive or negative deviations, but become apparent when the behaviour of the system approximates to Raoult's law.

The three solvents referred to above have dipole moments between 3 and 4 D, and molecular attraction is due largely to polar forces. Benzene and toluene, which have similarly small vapour-pressure deviations, show no inflexion. It is assumed, therefore, that inflexion in these curves is the result of variation in polar interactions with solvent concentration.

Influence of Temperature on Deviation.—Deviations at various temperatures are given in Table 4 for six solvents.

TABLE 4. *Deviation (%) for equimolecular mixtures at six temperatures.*

Solvent	−20°	−10°	−5°	0°	5°	10°	Solvent	−20°	−10°	−5°	0°	5°	10°
n-C_7H_{16} ...	—	62·5	59·5	55·5	51·5	48·5	$Me{\cdot}NO_2$ ...	—	— 6	—	~0	—	1·5
CCl_4	—	39	38	35	32	31	$(Me{\cdot}CO_2)O$	−32	−30	—	−28	—	−27
C_6H_6	—	—	11	9·5	8·5	—	$Me{\cdot}CO_2Et$	—	−37	−35	−34	−32	−30

Both negative and positive deviations diminish, *i.e.*, the systems move towards ideal, with increasing temperature. The change in deviation with temperature for acetic anhydride and ethyl acetate, though detectable, is small compared with the magnitude of the deviation, indicating that the energy of compound formation with dinitrogen tetroxide is small in the liquid state.

Dipole Moment–Vapour Pressure Correlation for Non-donors.—In determining the pressures in Fig. 4, the partial pressure of the solvent was assumed to be that proportion of its vapour pressure indicated by the mol. fraction of solvent. This was subtracted from the total observed pressure, and since the vapour pressures of the solvents used are small compared with that of dinitrogen tetroxide the difference gives the partial pressure of the tetroxide without appreciable error. The values so obtained (for 0°) are plotted in Fig. 4 against the dipole moment of the solvent. Five polar solvents of widely differing molecular structures show a correlation which is very close to linear, suggesting that for polar non-donor solvents the only forces of molecular attraction which have significance in tetroxide systems are those which can be expressed quantitatively in terms of dipole moment of the solvent. Values for the non-polar heptane do not correspond with those for the polar solvents.

Degree of Compound Formation with Donor Solvents.—Since compound formation rarely plays the predominant rôle in determining the physical properties of these mixtures, it is not at present possible to derive with accuracy from the vapour-pressure data the proportion of the molecules taking part in compound formation; the difficulties

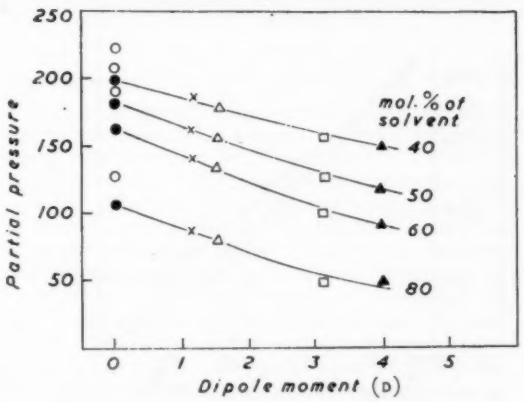

FIG. 4. *Correlation of dipole moment of solvent with partial pressure of* N_2O_4 (*mm.* Hg) *at* 0°.

● CCl_4, ○ *n*-C_7H_{16}, × $CHCl_3$, △ PhCl, □ Me·NO_2, ▲ $PhNO_2$.

encountered in a quantitative approach are defined briefly below. With certain assumptions, however, an estimate can be made. Thus, we may compare the observed partial pressure of the tetroxide ($P_{obs.}$) with that corresponding to a mixture containing a non-donor solvent whose molecule has an equal dipole moment (P_{dipole}, interpolated from Fig. 4). If the polar and electron-transfer forces are treated as additive (*i.e.*, if it is assumed that partial electron transfer to the tetroxide does not in itself seriously modify the dipole moment of the solvent molecule) then the ratio of the two pressures is a measure of the

TABLE 5.

Solvent	N	$P_{obs.}$ (mm.)	P_{dipole} (mm.)	N_2O_4 molecules combined * (%)
Me·CO_2Et	0·6	113	178	59
	0·5	82	153	62
	0·4	56	131	69
$(Me·CO)_2O$	0·6	126	166	44
	0·5	96	137	46
	0·4	74	113	47

* From $100x/N$ where $x = N(1 - P_{obs.}/P_{dipole})/(1 - NP_{obs.}/P_{dipole})$.

degree of compound formation, and in a mixture in which the initial mol. fraction of dinitrogen tetroxide is N, the mol. fraction of uncombined tetroxide is given by $N \times P_{obs.}/P_{dipole}$. It is clear, however, from the appearance of inflexion in some of the vapour-pressure curves that dipolar forces vary with concentration. These variations,

though small, are sufficiently large to prevent even an approximate assessment of compound formation when the deviation is small (as with methyl cyanide), and these effects also complicate any attempt to derive equilibrium constants over a concentration range. However, with donor solvents showing large negative deviations, these variations are relatively small, and some picture of the order of compound formation at 0° may be derived from the ratio $P_{obs.}/P_{dipole}$. Some typical observations are collected in Table 5.

In deriving these values the further assumption is made that with weak donors in the liquid state, the component ratio in the addition compound does not differ from unity.

The various assumptions mentioned are probably sufficiently correct to justify the general conclusion that with the strongest donor solvents used in this work, an equimolar mixture may be considered as equivalent to one in which approximately half the molecules present form addition compounds. In fact, since the environment of each tetroxide molecule will be the same, partial transfer of charge from each solvent to each tetroxide molecule occurs. If the maximum charge transfer corresponding to a stable addition compound be defined by a coefficient (resembling Mulliken's " charge-transfer reaction co-ordinate " [15]) of unity, then the state of the liquid mixtures discussed here is represented

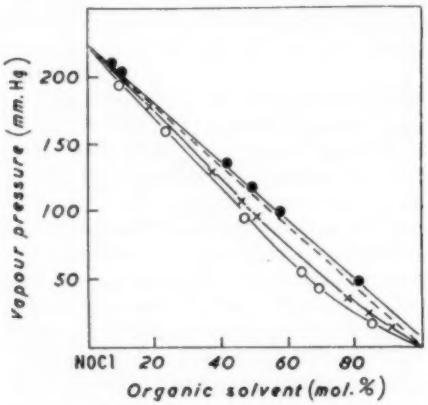

FIG. 5. *Vapour pressures of* NOCl–*organic solvent mixtures at* −30·8°.

● $CHCl_3$, × pyridine, ○ $Me{\cdot}CO_2Et$.
The broken line represents ideality.

by charge-transfer coefficients up to about 0·5, a degree of charge transfer which is apparently adequate to modify the chemical reactivity of the tetroxide.

Comparison with Nitrosyl Chloride Systems.—In view of its zero dipole moment, dinitrogen tetroxide is particularly convenient for the study of molecular interactions in the liquid state; vapour-pressure deviations can be considered in terms of the dipole moment of the solvent only, and negative deviations are only given by those solvents known to be capable of addition-compound formation. This is not the case in nitrosyl chloride systems, where the polar nature of nitrosyl chloride ($\mu = 1{\cdot}83$ D) gives rise to negative deviations in the absence of compound formation. Vapour pressures of three organic solvent–nitrosyl chloride mixtures are shown in Fig. 5, and values at other temperatures are collected in Table 6. The influence of this dipole is shown clearly in the mixtures with the non-donor chloroform. With dinitrogen tetroxide there is a positive deviation of 21% at 0°, whereas with nitrosyl chloride the system obeys Raoult's law almost exactly. Ethyl acetate (Fig. 5) shows a deviation of −18% with nitrosyl chloride at −30·8°, compared with −37% for dinitrogen tetroxide mixtures at −10°. The influence of the nitrosyl chloride dipole being allowed for, the vapour-pressure data provide no evidence for compound formation between ethyl acetate and nitrosyl chloride in the liquid state. The solid state has not been studied, but phase diagrams for another oxygen donor compound, dioxan, with nitrosyl chloride show no evidence for compound formation

[15] Mulliken, *J. Phys. Chem.*, 1952, **56**, 801.

in the solid state.[1a] The pyridine system shows only a small negative deviation (12% at −30·8°); this indicates negligible compound formation in the liquid state, though pyridine forms a solid compound with dinitrogen tetroxide at low temperatures.[2] This is consistent

TABLE 6. *Vapour pressures* (mm.) *of nitrosyl chloride–organic solvent mixtures.*

Chloroform (mol. %)	0	7·5	9·0	41·0	42·8	48·5	57·8	80·5	100
Temp.									
−21·2°	363	342	—	223	—	197	167	83	18
−40·7	131	125	120	80	77	69	59	30	4·5
−50·7	71·5	68	66	44	42	40	34	20	2·0
Ethyl acetate (mol. %)	9·0	23·0	47·5	64·0	68·8	85·0	100		
−21·2	332	266	156	94	72	34	6		
−40·7	118	92	55	32	24	11	3		
−50·7	64	53	29	17	13	6	~1		
Pyridine (mol. %)	7·4	18·0	37·2	45·6	50·0	77·4	84·2	90·8	100
−21·2	342	295	215	182	161	64	43	26	1
−40·7	122	103	76	63	58	23	15	10	~0

with other evidence that only the strongest donors (*e.g.*, some simple tertiary amines [16]) show evidence of compound formation with nitrosyl chloride in the liquid state.

EXPERIMENTAL

The mixtures (about 25 ml.) were made by direct weighing (with precautions against contact with atmosphere) into a glass bulb of about 25 ml. capacity. This was connected to a glass spiral gauge, and a side arm for evacuation, the vapour volume being about 25 ml. The spiral gauge was used with an optical lever with calibrated scale. The possible error in reading the scale corresponded to a pressure of ±0·5 mm. Hg. The gauge was employed mainly as a null-point instrument; the air pressure outside the spiral was adjusted, by a fine air-leak, until it approximately balanced the vapour pressure, and was measured by a mercury manometer. The vapour pressures were determined from the manometer reading with a correction for the slight deviation of the gauge scale reading from zero. The liquid mixture was degassed by successive freezing in liquid air, evacuation of the containing vessel to 0·002 mm. Hg, and warming to the temperature of the experiment. This was repeated until the vapour-pressure values were reproducible; two such operations were normally adequate. Ground-glass joints in the apparatus were lubricated with a little Silicone grease. Temperature was controlled by immersing that part of the bulb and leads which contained the liquid mixture and vapour phase in a 2-l. silvered Dewar vessel containing melting ice or solvent maintained at the correct temperature. Temperatures above −20° were measured by a calibrated mercury thermometer; below −20° an alcohol thermometer was used, calibrated with nitrosyl chloride by employing the vapour pressure values accurately determined by Partington and Whynes.[17]

The organic liquids used were carefully purified immediately before use, particular care being taken with the drying of the liquids. There was no visible evidence of chemical reaction between the tetroxide and the solvents during the experiments, but slight increases in pressure with time were observed in a few cases. With acetic acid and benzyl cyanide the change in pressure was negligible at −10° and below; at 10° the drift in pressure was of the order of 1 to 5 mm. Hg in 15 min. The accuracy of the vapour-pressure values reported is estimated as ±1 mm. Hg, and it was not necessary to apply a correction for the gaseous dissociation of the tetroxide into nitrogen dioxide at the low temperatures employed.

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THE UNIVERSITY, NOTTINGHAM. [*Received, September 27th,* 1956.]

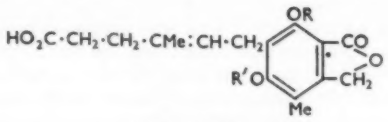
[16] Comyns, *Nature*, 1953, **172**, 491; *J.*, 1955, 1557.
[17] Partington and Whynes, *J. Phys. Chem.*, 1949, **53**, 500.

374. *Lactones. Part V.* Experiments relating to Mycophenolic Acid.*

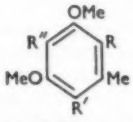
By W. R. Logan and G. T. Newbold.

The structure of mycophenolic acid has been confirmed as (I) by infrared spectroscopy and by the synthesis of the degradation product, 6-carboxymethyl-5 : 7-dimethoxy-4-methylphthalide (X; R = $CH_2 \cdot CO_2H$).

From degradative studies by Raistrick and his co-workers [1-4] the structure of mycophenolic acid, a metabolic product of strains of *Penicillium brevi-compactum*, is almost certainly structure (I). Birkinshaw, Raistrick, and Ross,[4] however, admitted slight doubts as to which of the two nuclear hydroxyl groups in normycophenolic acid (II) was methylated in mycophenolic acid and as to whether the potential hydroxymethyl group in the phthalide ring was *ortho* or *meta* to the nuclear methyl group. Though the fact that mycophenolic acid gives a ferric chloride colour † suggests the hydroxy-phthalide system given in structure (I), the phthalide carbonyl stretching frequency region of the infrared spectra shows maxima at 1742 ($CHCl_3$), 1748 (CCl_4), and 1751 cm.$^{-1}$ (dioxan) while the dimethoxy-compound (III) shows maxima at 1763, 1776, and 1770 cm.$^{-1}$ in the same solvents, respectively, clearly indicating intramolecular hydrogen bonding as expected from structure (I).[7]



(I) R = H, R′ = Me
(II) R = R′ = H
(III) R = R′ = Me



(IV) R = CO_2H, R′ = R″ = H
(V) R = CO_2H, R′ = Br, R″ = H
(VI) R = R″ = H, R′ = Br
(VII) R = H, R′ = Br, R″ = CO_2H

In order further to confirm the orientation of groups in the dimethoxyphthalide (III) it was aimed to synthesise 6-carboxymethyl-5 : 7-dimethoxy-4-methylphthalide (X; R = $CH_2 \cdot CO_2H$). This compound has been obtained [3] by ozonolysis of the dimethoxyphthalide (III) or by oxidation of the corresponding aldehyde with alkaline iodine. Our starting material was orsellinic acid dimethyl ether (IV); [8] this compound on treatment with 1½ mol. of bromine according to the photobromination technique [9] gave 3-bromo-4 : 6-dimethoxy-2-methylbenzoic acid (V) as major product. The orientation of the bromine atom was readily established by decarboxylation which gave 2-bromo-3 : 5-dimethoxytoluene (VI) which has been prepared by decarboxylation [10] of the acid (VII) and by bromination of orcinol followed by methylation.[11] On photobromination with 2 mol. of bromine followed by alkaline hydrolysis orsellinic acid dimethyl ether gave

* Part IV, *J.*, 1956, 4980.

† Mycophenolic acid [2] gives a blue colour; cf. 7-hydroxyphthalide [5] which gives a purple colour while 4-hydroxyphthalide [6] gives no colour.

[1] Clutterbuck, Oxford, Raistrick, and Smith, *Biochem. J.*, 1932, **26**, 1441.
[2] Clutterbuck and Raistrick, *ibid.*, 1933, **27**, 654.
[3] Birkinshaw, Bracken, Morgan, and Raistrick, *ibid.*, 1948, **43**, 216.
[4] Birkinshaw, Raistrick, and Ross, *ibid.*, 1952, **50**, 630.
[5] Blair, Brown, and Newbold, *J.*, 1955, 708.
[6] Buehler, Powers, and Michels, *J. Amer. Chem. Soc.*, 1944, **66**, 417.
[7] Duncanson, Grove, and Zealley, *J.*, 1953, 1331.
[8] Herzig, Wenzel, and Kurtzweil, *Monatsh.*, 1903, **24**, 894; Robertson and Robinson, *J.*, 1927, 2196.
[9] Eliel, Rivard, and Burgstahler, *J. Org. Chem.*, 1953, **18**, 1679; Eliel and Rivard, *ibid.*, 1952, **17**, 1252.
[10] Asahina and Fuzikawa, *Ber.*, 1934, **67**, 163; Fuzikawa, *Ber.*, 1935, **68**, 72.
[11] Chakravarti and Mukerjee, *J. Indian Chem. Soc.*, 1937, **14**, 725; Asahina and Fuzikawa, ref. 10.

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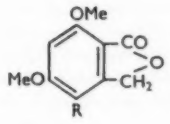
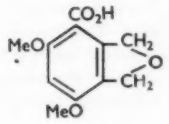
4-bromo-5 : 7-dimethoxyphthalide (VIII; R = Br) as principal product with some 3-bromo-4 : 6-dimethoxy-2-methylbenzoic acid. Photobromination of methyl orsellinate dimethyl ether with 2 mol. of bromine or of the methyl ester of the acid (V) with 1 mol. of bromine gave in good yield methyl 3-bromo-2-bromomethyl-4 : 6-dimethoxybenzoate, alkaline hydrolysis of which gave the phthalide (VIII; R = Br). The latter has also been prepared from orsellinic acid dimethyl ether by reaction with 1 mol. of *N*-bromosuccinimide to give the acid (V) whose methyl ester was treated with a further mol. of the reagent followed by hydrolysis. These results show that nuclear bromination must occur first and the presence of the *ortho*-bromo-group is necessary to activate the methyl group for side-chain bromination.

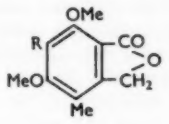
The phthalide (VIII; R = Br) on catalytic hydrogenation afforded 5 : 7-dimethoxyphthalide (VIII; R = H), alkaline permanganate oxidation of which gave the known 3 : 5-dimethoxyphthalic acid.[12] On chloromethylation at 0° by a modification of the method of Wilson *et al.*,[13] the phthalide (VIII; R = H) gave 4-chloromethyl-5 : 7-dimethoxyphthalide (VIII; R = CH_2Cl). The position of the entering chloromethyl group was proved by the ability of corresponding hydroxymethyl compound (VIII; R = CH_2·OH), formed from the chloromethyl compound (VIII; R = CH_2Cl) by hydrolysis with aqueous carbonate, to be rearranged [14] by methanolic sodium methoxide to 5 : 7-dimethoxyphthalan-4-carboxylic acid (IX) which was also formed during the hydrolysis with carbonate. Reductive dehalogenation of the chloromethyl compound (VIII; R = CH_2Cl) gave 5 : 7-dimethoxy-4-methylphthalide (VIII; R = Me) into which a 6-chloromethyl group was introduced by vigorous chloromethylation forming 6-chloro-



(VIII)



(IX)



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methyl-5 : 7-dimethoxy-4-methylphthalide (X; R = CH_2Cl) which reacted readily with potassium cyanide to yield 6-cyanomethyl-5 : 7-dimethoxy-4-methylphthalide (X; R = CH_2·CN), alkaline hydrolysis of which afforded 6-carboxymethyl-5 : 7-dimethoxy-4-methylphthalide (X; R = CH_2·CO_2H). This acid was identical with that obtained by degradation of mycophenolic acid methyl ether.

Hydrolysis of the chloromethylphthalide (X; R = CH_2Cl) with aqueous sodium carbonate gave 6-hydroxymethyl-5 : 7-dimethoxy-4-methylphthalide (X; R = CH_2·OH) which on oxidation with chromic acid gave the corresponding aldehyde (X; R = CHO), m. p. 131·5—133°; while it has not been possible to make a direct comparison between the synthetic aldehyde and a crystalline sample of that, m. p. 125—126°, obtained [3] by Birkinshaw *et al.*, as end product of the side-chain degradation of the dimethoxyphthalide (III), we feel that the latter authors' aldehyde was incompletely purified.

The same conclusion regarding the structure of mycophenolic acid has been reached independently by Professor A. J. Birch,[15] whose helpful co-operation we acknowledge.

Experimental

Ultraviolet absorption spectra were determined in ethanol.

Orsellinic Acid Dimethyl Ether (4 : 6-*Dimethoxy*-2-*methylbenzoic Acid*).—Ethyl everninate

[12] Fritsch, *Annalen*, 1897, **296**, 344.
[13] Cf. Wilson, Zirkle, Anderson, Stehle, and Ullyot, *J. Org. Chem.*, 1951, **16**, 792.
[14] Cf. Brown and Newbold, *J.*, 1952, 4878; Blair and Newbold, *J.*, 1954, 3935; Blair, Logan, and Newbold, *J.*, 1956, 3608.
[15] Birch and Massy-Westropp, personal communication.

(5·84 g.), prepared [17] from ethyl orsellinate [16] in 71% yield, was heated on the steam-bath for 1¼ hr. with aqueous sodium hydroxide (58 c.c.; 2N). The cooled solution was stirred with dimethyl sulphate (2·5 c.c.). After 1½ hr. dimethyl sulphate (2·5 c.c.) was added and thereafter five additions of dimethyl sulphate (each 2·5 c.c.) together with aqueous sodium hydroxide (each 11 c.c.; 2N) were made at hourly intervals. 2 hr. after the last addition, aqueous sodium hydroxide (11 c.c.; 2N) was added and the solution refluxed for 1½ hr. The cooled solution was acidified (Congo red) with hydrochloric acid (*d*, 1·15). The orsellinic acid dimethyl ether (5·2 g.) crystallised from aqueous ethanol as plates, m. p. **142—143°** (lit.,[8] m. p. **143—144°**).

3-Bromo-4 : 6-dimethoxy-2-methylbenzoic Acid.—(*a*) A partial solution of orsellinic acid dimethyl ether (1·0 g.) in dry carbon tetrachloride (25 c.c.), heated under reflux and irradiated by a 150 w lamp, was treated dropwise with bromine (0·527 c.c.; 2 mol.) during 10 min. and refluxing continued for 1½ hr. The solvent was removed under reduced pressure and the solid residue heated under reflux for 3 hr. with aqueous sodium hydroxide (50 c.c.; 2N). The cooled solution was extracted with chloroform (50 c.c.) and acidified (Congo red) with hydrochloric acid (*d*, 1·15). The precipitate was extracted with chloroform (3 × 50 c.c.) and the extract (*A*) washed with aqueous sodium hydrogen carbonate (3 × 50 c.c.; 10%). Acidification of the aqueous washings gave *3-bromo-4 : 6-dimethoxy-2-methylbenzoic acid* (0·48 g.) which separated from aqueous ethanol as needles, m. p. 210° (decomp.) (Found : C, 43·7; H, 4·0%; equiv., 276. $C_{10}H_{11}O_4Br$ requires C, 43·65; H, 4·0%; equiv., 275). Light absorption : max. at 2070 (ε = 34,000) and 2860 Å (ε = 3550). The *methyl ester*, prepared with diazomethane, crystallised from aqueous methanol as needles, m. p. 120—121° (Found : C, 45·5; H, 4·7. $C_{11}H_{13}O_4Br$ requires C, 45·7; H, 4·5%), light absorption max. at 2065 (ε = 32,000) and 2895 Å (ε = 3350). Photobromination of orsellinic acid dimethyl ether (1·0 g.) with bromine (0·395 c.c.; 1·5 mol.) gave the bromo-acid (0·74 g.).

(*b*) (With Dr. JOHN BLAIR). A solution of orsellinic acid dimethyl ether (300 mg.) in carbon tetrachloride (20 c.c.) and benzene (10 c.c.) was refluxed with *N*-bromosuccinimide (1·05 mol.) for 5 hr. with irradiation from a 60 w lamp. The cooled reaction mixture was evaporated and the residual solid shaken with ether and aqueous sodium hydrogen carbonate (10%). Acidification of the aqueous phase and crystallisation of the precipitate from aqueous ethanol gave the bromo-acid (100 mg.), m. p. 210—211° (decomp.) alone or mixed with preparation from (*a*) (Found : C, 43·65; H, 4·0%).

Methyl 3-Bromo-2-bromomethyl-4 : 6-dimethoxybenzoate.—A solution of methyl 3-bromo-4 : 6-dimethoxy-2-methylbenzoate (250 mg.) in carbon tetrachloride (10 c.c.) was photobrominated as in (*a*) above with bromine (0·138 g.; 1 mol.). Refluxing was continued for 1 hr. after addition had been completed. Removal of the solvent gave an oil which rapidly solidified. Crystallisation from light petroleum (b. p. 60—80°) gave *methyl 3-bromo-2-bromomethyl-4 : 6-dimethoxybenzoate* (300 mg.) as needles, m. p. 118·5—119° (Found : C, 36·3; H, 3·5. $C_{11}H_{12}O_4Br_2$ requires C, 35·9; H, 3·3%), light absorption : max. at 2200 (ε = 25,000) and 3070 Å (ε = 3900). The same compound, m. p. and mixed m. p. 118—119°, was obtained in almost quantitative yield by photobromination of methyl orsellinate dimethyl ether with bromine (2 mol.).

4-Bromo-5 : 7-dimethoxyphthalide.—(i) The foregoing bromomethyl compound (0·6 g.) was refluxed with aqueous sodium hydroxide (25 c.c.; 2N) for 2 hr. The almost complete solution was cooled, extracted once with chloroform (25 c.c.) and the aqueous phase acidified (Congo red) with hydrochloric acid (*d*, 1·15); the resulting precipitate was extracted with chloroform (50 c.c.), and the extract washed with aqueous sodium hydrogen carbonate (2 × 25 c.c.) and water (25 c.c.) and dried (Na_2SO_4). Evaporation of the chloroform and crystallisation of the solid from chloroform–methanol gave *4-bromo-5 : 7-dimethoxyphthalide* (330 mg.) as fine needles, m. p. 246—248° (Found : C, 44·5; H, 3·5. $C_{10}H_9O_4Br$ requires C, 44·0; H, 3·3%). Light absorption max. at 2205 (ε = 35,400), 2590 (ε = 12,400), and 2985 Å (ε = 5900). It showed a strong infrared band at 1767 cm.$^{-1}$ in chloroform (phthalide carbonyl stretching frequency). The photobromination of orsellinic acid dimethyl ether (1 g.) with 1½ mol. of bromine gave the bromophthalide (0·29 g.). (ii) The chloroform extract *A*, above, was washed with water, dried (Na_2SO_4), and evaporated, and the residue hydrolysed as in (i). The bromo-phthalide thus obtained (0·6 g.) separated from chloroform–methanol as needles, m. p. and mixed m. p. 246—248° (Found : C, 44·2; H, 3·4%). (iii) Methyl 3-bromo-4 : 6-dimethoxy-2-methylbenzoate

[16] St. Pfau, *Helv. Chim. Acta*, 1933, **16**, 282.
[17] Fischer and Hoesch, *Annalen*, 1912, **391**, 347.

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(250 mg.) in carbon tetrachloride (10 c.c.) and benzene (10 c.c.) was heated under reflux and irradiated by a 150 w lamp for 1½ hr. with *N*-bromosuccinimide (162 mg.; 1·05 mol.). The mixture was evaporated to dryness under reduced pressure and the residue refluxed for 2 hr. with aqueous sodium hydroxide (20 c.c.; 2N). The filtered solution was treated as in (i) to give the bromo-phthalide (66 mg.) as needles, m. p. and mixed m. p. 243·5—244·5°, from chloroform–methanol. From the bicarbonate washings the bromo-acid (129 g.), m. p. 206·5—207°, was recovered.

2-Bromo-3 : 5-dimethoxytoluene.—3-Bromo-4 : 6-dimethoxy-2-methylbenzoic acid (200 mg.) was heated with quinoline (5 c.c.) and copper powder (100 mg.) at 210—230° (bath temp.) for 1 hr. The cooled mixture was diluted with ether (20 c.c.) and the ethereal solution successively washed with 3N-hydrochloric acid, 10% aqueous sodium hydroxide, and water and dried (Na_2SO_4). Removal of the ether gave a light-brown oil which solidified. Crystallisation from aqueous ethanol followed by sublimation at 70°/10^{-3} mm. gave 2-bromo-3 : 5-dimethoxytoluene (60 mg.), m. p. 53·5—54·5° undepressed on mixing with a synthetic specimen,[10] m. p. 51° (lit., 57°).

5 : 7-Dimethoxyphthalide.—A suspension of 4-bromo-5 : 7-dimethoxyphthalide (1·56 g.) in dry ethyl acetate (250 c.c.) was shaken with hydrogen at room temperature and pressure in the presence of palladised charcoal (1·2 g.; 2½% of palladium chloride on charcoal) and magnesium oxide (3·0 g.). When absorption was complete (*ca.* 12 hr.) the mixture was filtered (filtrate *B*) and the insoluble material extracted with boiling chloroform (3 × 100 c.c.). The combined extracts and filtrate *B* were evaporated to give a solid which crystallised from chloroform–methanol to give *5 : 7-dimethoxyphthalide* (1·02 g.) as stout needles, m. p. 151—153° (Found : C, 61·5; H, 5·25. $C_{10}H_{10}O_4$ requires C, 61·85; H, 5·2%), light absorption : max. at 2165 (ε = 37,600), 2560 (ε = 15,900), and 2900 Å (ε = 5300).

3 : 5-Dimethoxyphthalic Acid.—A solution of 5 : 7-dimethoxyphthalide (50 mg.) in hot aqueous sodium hydroxide (10 c.c.; 2N) was treated with aqueous potassium permanganate (4·6 c.c.; 5%). After being heated on the steam-bath for 10 min., the mixture was cooled and filtered. The filtrate and washings were evaporated to small bulk under reduced pressure and acidified (Congo red) with hydrochloric acid (*d*, 1·15) to give 3 : 5-dimethoxyphthalic acid (50 mg.) as needles, m. p. 159° (decomp.) alone or mixed with an authentic sample [lit.,[12] m. p. 158° (decomp.)].

4-Chloromethyl-5 : 7-dimethoxyphthalide.—5 : 7-Dimethoxyphthalide (100 mg.) was suspended in hydrochloric acid (0·2 c.c.; *d*, 1·15) and aqueous formaldehyde (0·1 c.c.; 40%), and the mixture treated with dry hydrogen chloride at 0° for 35 min. After being kept overnight at room temperature the solid was triturated with water and extracted with chloroform. The extract was washed with water, dried (Na_2SO_4), and evaporated and the solid crystallised from ethyl acetate–light petroleum (b. p. 60—80°) to give *4-chloromethyl-5 : 7-dimethoxyphthalide* (110 mg.) as prisms, m. p. 187·5—189° (Found : C, 54·4; H, 4·7. $C_{11}H_{11}O_4Cl$ requires C, 54·45; H, 4·6%), light absorption : max. at 2240 (ε = 38,000), 2590 (ε = 14,400), and 2950 Å (ε = 5000).

4-Hydroxymethyl-5 : 7-dimethoxyphthalide.—4-Chloromethyl- 5 : 7-dimethoxyphthalide (147 mg.) was refluxed for 1½ hr. with a solution of sodium carbonate (480 mg.) in water (10 c.c.). The solution was worked up as described for analogous cases by Blair and Newbold [14] and the lactone fraction crystallised from ethanol to give *4-hydroxymethyl-5 : 7-dimethoxyphthalide* (48 mg.) as needles, m. p. 233·5—240° (Found : C, 59·15; H, 5·4. $C_{11}H_{12}O_5$ requires C, 58·9; H, 5·4%), light absorption : max. at 2210 (ε = 35,000), 2580 (ε = 13,800), and 2930 Å (ε = 6150).

5 : 7-Dimethoxyphthalan-4-carboxylic Acid.—(*a*) The acid fraction from the foregoing experiment, crystallised from ethyl acetate, gave the acid (51 mg.) as short needles, m. p. 221—222·5° (Found : C, 59·2; H, 5·6. $C_{11}H_{12}O_5$ requires C, 58·9; H, 5·4%), light absorption : max. at 2160 (ε = 26,000), 2550 (ε = 10,400) and 2945 Å (ε = 4400).

(*b*) 4-Hydroxymethyl-5 : 7-dimethoxyphthalide (110 mg.) was refluxed with methanolic sodium methoxide [from sodium (50 mg.) and dry methanol (10 c.c.)] for 7½ hr. The acid was isolated as described for an analogous case by Blair, Logan, and Newbold.[14] It separated from ethyl acetate as needles, m. p. 221—222° alone or mixed with the preparation from (*a*).

5 : 7-Dimethoxy-4-methylphthalide.—4-Chloromethyl-5 : 7-dimethoxyphthalide (200 mg.) was shaken in dry ethyl acetate (50 c.c.) with hydrogen at room temperature and pressure in the presence of palladised charcoal (174 mg.; 2·5% of palladium chloride on charcoal) and magnesium oxide

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(400 mg.). Hydrogen uptake was complete in 4½ hr. The reaction mixture was filtered and the residue well washed with boiling ethyl acetate; the filtrate and washings were evaporated and the residue, crystallised from ethyl acetate–light petroleum (b. p. 60—80°), gave the *phthalide* (160 mg.) as prismatic needles, m. p. 202—203° (Found: C, 63·1; H, 5·6. $C_{11}H_{12}O_4$ requires C, 63·45; H, 5·8%), light absorption: max. at 2220 (ε = 31,000), 2600 (ε = 14,000), and 2970 Å (ε = 7200).

6-*Chloromethyl*-5: 7-*dimethoxy*-4-*methylphthalide*.—5: 7-Dimethoxy-4-methylphthalide (200 mg.) was refluxed for 1 hr. with aqueous formaldehyde (2·06 c.c.; 40%) and hydrochloric acid (3·44 c.c.; *d*, 1·15), dissolution being accompanied by separation of a brown oil. The mixture was cooled, diluted with water (30 c.c.), and extracted with chloroform (3 × 50 c.c.); the combined extracts were washed with aqueous sodium hydrogen carbonate (2 × 30 c.c.; 10%) and water, and dried (Na_2SO_4). Removal of the chloroform gave a yellow gum which crystallised from benzene–light petroleum (b. p. 60—80°) to give 6-*chloromethyl*-5: 7-*dimethoxy*-4-*methylphthalide* (150 mg.) as needles, m. p. 107—107·5°; the compound sublimed at 100°/10^{-3} mm. (Found: C, 56·8; H, 5·35. $C_{12}H_{13}O_4Cl$ requires C, 56·15; H, 5·1%), light absorption: max. at 2210 (ε = 40,000), 2450 (ε = 8600), and 2960 Å (ε = 2400).

6-*Cyanomethyl*-5: 7-*dimethoxy*-4-*methylphthalide*.—A solution of 6-chloromethyl-5: 7-dimethoxy-4-methylphthalide (200 mg.) in ethanol (10 c.c.) was added during ½ hr. to a cold solution of potassium cyanide (65 mg.) in water (1 c.c.) and the mixture heated on the steam-bath for 4 hr. The cooled mixture was filtered and the filtrate and ethanol washings were acidified (Congo red) with hydrochloric acid (*d*, 1·15). The filtered solution was concentrated to *ca.* 5 c.c. and diluted with water. The precipitate was washed with aqueous ethanol and crystallised from benzene–light petroleum (b. p. 60—80°) to give the *cyanomethyl compound* (96 mg.) as needles, m. p. 129—131·5° (Found: C, 63·2; H, 5·3. $C_{13}H_{13}O_4N$ requires C, 63·15; H, 5·3%), light absorption: max. at 2140 (ε = 41,000), 2460 (ε = 10,000), and 2915 Å (ε = 3150). The compound shows a weak band at 2222 cm.$^{-1}$ in carbon tetrachloride (C≡N stretching frequency).

6-*Carboxymethyl*-5: 7-*dimethoxy*-4-*methylphthalide*.—The foregoing cyanomethyl compound (60 mg.) was refluxed for 2 hr. with aqueous potassium hydroxide (10 c.c.; 10%). The cooled solution was acidified (Congo red) with hydrochloric acid (*d*, 1·15) and the precipitate extracted with chloroform (2 × 20 c.c.). Isolation through aqueous sodium hydrogen carbonate gave the *acid* (47 mg.) which separated from benzene–light petroleum (b. p. 60—80°) as needles, m. p. 152—153° (Found: C, 58·6; H, 5·5. $C_{13}H_{14}O_6$ requires C, 58·6; H, 5·3%), light absorption: max. at 2160 (ε = 43,000), 2500 (ε = 11,000), and 2930 Å (ε = 3300). The acid on being mixed with 6-carboxymethyl-5: 7-dimethoxy-4-methylphthalide, m. p. 152—153° (lit.,[3] m. p. 153°), obtained by degradation of mycophenolic acid methyl ether, had m. p. 152—153° and the infrared spectra of both acids determined in Nujol were identical. The methyl esters, prepared with diazomethane and crystallised from methanol had m. p. 92—93·5° (synthetic) and 93—94° (from degradation; lit.,[3] 94—95°) and were undepressed on mixing.

6-*Hydroxymethyl*-5: 7-*dimethoxy*-4-*methylphthalide*.—6-Chloromethyl-5: 7-dimethoxy-4-methylphthalide (69 mg.) was refluxed with aqueous sodium carbonate (10 c.c.; 10%) for 1 hr. The cooled solution was filtered and acidified (Congo red) and the product isolated with chloroform. The *hydroxymethyl compound* (50 mg.) separated from benzene–light petroleum (b. p. 60—80°) as needles, m. p. 103—104° (Found: C, 60·5; H, 6·3. $C_{12}H_{14}O_5$ requires C, 60·5; H, 5·9%), light absorption: max. at 2150 (ε = 31,000), 2490 (ε = 7500), and 2935 Å (ε = 2500).

6-*Formyl*-5: 7-*dimethoxy*-4-*methylphthalide*.—A solution of crude 6-hydroxymethyl-5: 7-dimethoxy-4-methylphthalide (420 mg.) in acetic acid (20 c.c.) was treated, at room temperature with stirring, during 3 min. with a solution of chromium trioxide (500 mg.) in acetic acid (10 c.c.). 5 min. after the addition had been completed the solution was diluted with water (20 c.c.) and extracted with chloroform (3 × 30 c.c.). The combined extract was washed with aqueous sodium hydrogen carbonate (2 × 80 c.c.; 10%) and water, and dried (Na_2SO_4). Removal of the chloroform gave a yellow gum which rapidly solidified. The solid was extracted with boiling light petroleum (b. p. 60—80°) and thrice crystallised from this solvent, separating as needles. Sublimation at 100°/10^{-3} gave 6-*formyl*-5: 7-*dimethoxy*-4-*methylphthalide* (60 mg.), m. p. 131·5—133° (Found: C, 60·9; H, 5·2. $C_{12}H_{12}O_5$ requires C, 61·0; H, 5·1%), light absorption: max. at 2320 (ε = 28,000) and 3100 (ε = 2700) and inflexion at 2040—2100 Å (ε = 13,000).

We gratefully acknowledge the assistance of Mr. J. G. C. Campbell and his staff of the Department of Microbiology in obtaining mycophenolic acid. Analyses were performed by Dr. A. C. Syme and Mr. W. McCorkindale and spectra determined by Miss P. Adams (ultraviolet) and Miss N. Caramando (infrared). Professor H. Raistrick, F.R.S., kindly supplied cultures of *Penicillium brevi-compactum*.

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375. *A Comparison of* iso*Lichenin and Lichenin from Iceland Moss* (Cetraria islandica).

By N. B. CHANDA, E. L. HIRST, and D. J. MANNERS.

Purified *iso*lichenin and lichenin, from Iceland moss, have been characterised by methylation and periodate oxidation.

*iso*Lichenin has been found to consist solely of D-glucose residues united by α-1 : 3- and α-1 : 4-glucosidic linkages which are present in the relative proportion of 3 : 2. The molecule appears to be linear, with an average chain length of 42—44 glucose residues. The structure of lichenin as a linear polymer of β-D-glucose containing both 1 : 3- and 1 : 4-linkages in the proportion of 3 : 7 has been confirmed.

SEVERAL structural investigations of the polysaccharides of lichens, which are symbiotic organisms in the phylum *Thallophyta*, have been reported recently. The major polysaccharide in Iceland moss (*Cetraria islandica*) is lichenin, which was shown by Meyer and Gürtler [1] to contain D-glucose residues united by 1 : 3- and 1 : 4-linkages. In addition, Iceland moss contains *iso*lichenin and hemicelluloses. The latter are composed of D-galactose, D-mannose, and uronic acid residues.[2] Lichenin and *iso*lichenin, from the Indian lichens *Usnea longissima* and *Roccella montagnei* respectively, are both polymers of D-glucose, although they differ in physical and chemical properties.[3] Pustulan, from *Umbilicaria pustulata*, is a linear glucan in which the component residues are united by β-1 : 6-linkages.[4] In contrast, the alkali-soluble polysaccharides of reindeer moss (*Cladonia alpestris*) are highly branched molecules composed of D-galactose, D-glucose, and D-mannose residues.[5] In this communication, a structural investigation of *iso*lichenin from Iceland moss is described, and previous observations on the structure of lichenin have been confirmed and extended.

iso*Lichenin*.—The presence of *iso*lichenin in Iceland moss has been known for many years. This polysaccharide differs markedly from lichenin in being freely soluble in water, giving a dextrorotatory solution, which is stained blue by iodine. Pringsheim [6] concluded that *iso*lichenin was a glucan related to amylose, but Karrer [7] and Meyer [8] and their co-workers considered it to be a mixture of polysaccharides derived from glucose, galactose, and mannose. Attempts to purify *iso*lichenin were, in general, unsuccessful. In the present study it has been found that *iso*lichenin is, in fact, composed solely of glucose residues.

Iceland moss, freed from fatty materials and lichen acids, was extracted with boiling water. The impure lichenin which came down on cooling was removed and smaller amounts of this polysaccharide were then separated by alternate freezing and thawing

[1] Meyer and Gürtler, *Helv. Chim. Acta*, 1947, **30**, 751.
[2] Buston and Chambers, *Biochem. J.*, 1933, **27**, 1691.
[3] Mittal and Seshadri, *J. Sci. Ind. Res., India*, 1954, **13**, *B*, 244; *ibid.*, 1954, **13**, *A*, 174.
[4] Lindberg and McPherson, *Acta Chem. Scand.*, 1954, **8**, 985.
[5] Aspinall, Hirst, and Warburton, *J.*, 1955, 651.
[6] Pringsheim, *Ber.*, 1924, **57**, 1581.
[7] Karrer and Joos, *Z. physiol. Chem.*, 1924, **141**, 311.
[8] Meyer and Gürtler, *Helv. Chim. Acta*, 1947, **30**, 761.

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of the solution. Other contaminating polysaccharides were removed as insoluble alkaline-copper complexes, and further purification was effected by fractional precipitation with acetone of the water-soluble copper complex of *iso*lichenin. After dialysis and treatment with ion-exchange resins, the purified *iso*lichenin was precipitated by alcohol. From 6 kg. of Iceland moss, 2·7 g. of pure *iso*lichenin were finally obtained.

On acid hydrolysis, *iso*lichenin was converted almost quantitatively into glucose. The presence of other sugars and uronic acids could not be demonstrated. In water *iso*lichenin had an unusually high positive rotation ($[\alpha]_D$ +255°) which may be attributed to α-1 : 3-linked glucopyranose residues (compare nigeran,[9] $[\alpha]_D$ +270° to +283° in N-sodium hydroxide). The *iso*lichenin showed slight reducing action towards alkaline hypoiodite (apparent D.P. 34). The aqueous solution gave a greenish-blue colour with very dilute iodine solution (absorption $\lambda_{max.}$ at 600 mμ), but the " blue value "[10] was too low to permit accurate measurement (B.V. *ca.* 0·01 ; cf. *ca.* 1·30 for amylose and *ca.* 0·10 for amylopectin). The *iso*lichenin reduced 0·4 mole of sodium metaperiodate per glucose residue, indicating that some 60% of the glucose residues were unattacked by periodate. The formic acid produced by potassium metaperiodate oxidation corresponded to 1 mole per 14 glucose residues. If (see below) *iso*lichenin is a linear glucan, and the non-reducing and reducing end-groups give rise to one and two molecules of formic acid respectively, this would be equivalent to an average chain length of 42 glucose residues.

Hydrolysis of the methylated polysaccharide (OMe, 44·4%) gave 2 : 4 : 6- and 2 : 3 : 6-tri-*O*-methyl-D-glucose together with small amounts of 2 : 3 : 4 : 6-tetra- and mixed di-*O*-methyl-D-glucoses. The latter (*ca.* 2%) most probably arose from undermethylation of the polysaccharide (a tri-*O*-methyl glucan has OMe, 45·6%) and from hydrolytic demethylation. The proportion of tetra-*O*-methyl-D-glucose in the products of hydrolysis indicated the presence of 1 non-reducing terminal group per 44 glucose residues. Analysis of the tri-*O*-methylglucose fraction showed that 2 : 4 : 6-tri-*O*-methyl-D-glucose was the major component. From this evidence, and that previously cited, it is concluded that the molecule of *iso*lichenin is unbranched, and contains *ca.* 60% of α-1 : 3- and 40% of α-1 : 4-glucosidic linkages.

Measurements of the viscosity of solutions of *iso*lichenin acetate in chloroform indicated a low molecular weight, the D.P. being of the order of 40—50 glucose residues.

*iso*Lichenin was not attacked by barley or soya-bean β-amylase and it follows that α-1 : 3-glucosidic linkages must be situated near the non-reducing end of the molecule. This evidence makes it clear also that the *iso*lichenin investigated could not be a mixture of an amylose and an α-1 : 3-glucan.

The demonstration of α-1 : 3-glucosidic linkages in *iso*lichenin reveals an unusual structural feature in this glucan, and differentiates it from amylose (compare ref. 6). *iso*-Lichenin thus resembles nigeran, the intracellular polysaccharide synthesised by a strain of *Aspergillus niger*, which contains approximately equal numbers of α-1 : 3- and α-1 : 4-glucosidic linkages.[9] The analogy, however, is not complete in that the average chain length of nigeran is 300—350 glucose residues, and the detailed structures must differ since the proportion of 1 : 3- and 1 : 4-linked residues in *iso*lichenin does not permit an alternating sequence of these linkages such as is present in nigeran.

Lichenin.—Earlier investigations had established a structural similarity between lichenin and cellulose. For example, on acetolysis, cellobiose octa-acetate is formed,[11] and on methanolysis of the methylated polysaccharides, methyl 2 : 3 : 6-tri-*O*-methyl-D-glucoside is obtained,[12] although in both cases the yields from lichenin were smaller than those from cellulose. Nevertheless, lichenin differs from cellulose in being soluble in hot water,[13] and more susceptible to enzymic degradation. In 1947, Meyer and Gürtler [1]

[9] Barker, Bourne, and Stacey, *J.*, 1953, 3084.
[10] Bourne, Haworth, Macey, and Peat, *J.*, 1948, 924.
[11] Karrer, Joos, and Staub, *Helv. Chim. Acta*, 1923, **6**, 800.
[12] Karrer and Nishida, *ibid.*, 1924, **7**, 363.
[13] Haworth, *Chem. and Ind.*, 1939, 925.

provided the first clear evidence of a chemical difference between these polysaccharides. Hydrolysis of methylated lichenin gave tetra-*O*-methyl-D-glucose (0·6%, equivalent to an average chain length of *ca.* 170 glucose residues), and a mixture of 2 : 3 : 6- and 2 : 4 : 6-tri-*O*-methyl-D-glucose, thereby indicating the presence of both 1 : 4- and 1 : 3-linkages. Periodate oxidation showed that *ca.* 27% of 1 : 3-linkages were present. The relative proportions of 1 : 3- and 1 : 4-linkages in lichenin were confirmed by Boissonnas.[14]

In the present investigation two samples of lichenin have been studied. They were composed of D-glucose residues (94—96%) united by β-linkages, as shown by the specific rotation ($[\alpha]_D$ +8° to +10° in N-sodium hydroxide) and by hydrolysis to glucose by exo-β-glucosidase preparations * from *Helix aspersa* and almond emulsin. Partial hydrolysis, with dilute acid or with endo-β-glucosidase preparations from malted barley and *Cladophora rupestris*,[15] gave a series of sugars including glucose, cellobiose, laminaribiose, and higher oligosaccharides (paper chromatography). On periodate oxidation, 0·7 mole of periodate per anhydroglucose unit was consumed.

Chromatographic analysis of a hydrolysate of a methylated lichenin showed the presence of (*a*) tetra-*O*-methyl-D-glucose equivalent to an average chain length of 62 glucose residues, (*b*) 2 : 4 : 6-tri- (*ca.* 30%) and 2 : 3 : 6-tri-*O*-methyl-D-glucose (*ca.* 70%), thus confirming the presence of 1 : 3-linkages, and (*c*) no more than a trace of di-*O*-methyl-D-glucoses, showing the virtual absence of branch points. This sample of lichenin has, therefore, a shorter chain length than that examined by Meyer and Gürtler [1] and this difference probably arises from the more extensive fractionation of the lichen polysaccharides in the present study.

Lichenin does not appear to be a mixture of a β-1 : 3- and a β-1 : 4-glucan. A lichenin acetate was prepared, fractionated, and deacetylated. The regenerated polysaccharide consumed 0·7 mol. of periodate per anhydroglucose residue, indicating that no preferential removal of material containing a larger proportion of 1 : 3-linked glucose residues had occurred. Furthermore, treatment of periodate-oxidised lichenin with *iso*nicotinhydrazide or thiosemicarbazide gave the corresponding polymers,[16] and analysis of these (for N) gave values for the α-glycol content of lichenin similar to those previously obtained. If lichenin was chemically heterogeneous, then a complex of a periodate-oxidised β-1 : 4-glucan would be formed, with a correspondingly higher N content (cf. Barry and his co-workers [16]).

The 1 : 3-linkages appear to be randomly situated in the lichenin molecule. Periodate-oxidised lichenin was reduced to the corresponding polyalcohol with potassium borohydride, and partially hydrolysed with acid. Paper chromatography of the hydrolysate showed the presence of glucose but not of laminaribiose. It is concluded from this evidence that few, if any, sequences of two or more adjacent 1 : 3-linkages were present in the periodate-oxidised lichenin.

The lichenin from Iceland moss is therefore similar to the β-glucans isolated recently from barley [17] and oats,[18] although the relative proportions of 1 : 3- and 1 : 4-linkages and average chain lengths are not identical. Barley β-glucan (D.P. *ca.* 100) contains a higher proportion of 1 : 3-linkages (*ca.* 50%) than oat β-glucan (D.P. *ca.* 180: 33%) and lichenin.

Experimental

Analytical Methods.—The methods used were those described in earlier papers.[19] The following solvents were used for the paper chromatography of (*a*) unsubstituted sugars, and

* Exo-β-glucosidases cause a stepwise hydrolysis of successive linkages in a β-glucan, in contrast to endo-β-glucosidases, which catalyse random hydrolysis.

[14] Boissonnas, *Helv. Chim. Acta*, **1947**, **30**, 1703.
[15] Duncan, Manners, and Ross, *Biochem. J.*, 1956, **63**, 44.
[16] Barry, McCormick, and Mitchell, *J.*, 1954, 3692.
[17] Aspinall and Telfer, *J.*, 1954, 3519.
[18] Acker, Diemair, and Samhammer, *Z. Lebensm.-Untersuch.*, 1955, **100**, 180; **102**, 225.
[19] Manners and Khin Maung, *J.*, 1955, 867; Fleming, Hirst, and Manners, *J.*, 1956, 2831.

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(*b*) methylated sugars : butan-1-ol–benzene–pyridine–water [5 : 1 : 3 : 3, v/v; (*a*)], butan-1-ol–ethanol–water [4 : 1 : 5, v/v; (*a*) and (*b*)], and ethyl acetate–pyridine–water [10 : 4 : 3, v/v; (*a*)].

iso*Lichenin*

Isolation of iso*Lichenin*.—Iceland moss (500 g.), after extraction with benzene and methanol (Soxhlet) to remove waxy materials, was treated with cold 2% sodium carbonate solution (1·5 l.) to remove lichen acids. The moss residue was washed free from alkali, and extracted with boiling water (3 l.) for 2—3 hr. After filtering, the solution was allowed to cool slowly. Lichenin was precipitated, and was separated by centrifugation. The solution was concentrated and centrifuged, and residual lichenin removed by repeated freezing and thawing of the solution, the lichenin being partially precipitated during the thawing. Crude *iso*lichenin was isolated by precipitation with acetone, dissolution in cold 1% hydrochloric acid, and reprecipitation with acetone. The product, *iso*lichenin A, had $[\alpha]_D^{17}$ +165° (*c* 0·62 in H_2O) and contained glucose together with small amounts of galactose, mannose, and a pentose. From a total of 4 kg. of moss, 5·2 g. of *iso*lichenin A were obtained. The *iso*lichenin was treated with Fehling's solution, and the copper complex shaken with water (only two-thirds of the complex dissolved). The insoluble material, after regeneration to the polysaccharide with acetic acid, gave, on acid hydrolysis, mannose and galactose and a small amount of glucose. The polysaccharide regenerated from the soluble fraction [Fraction A; yield 2·8 g.] contained glucose and only traces of mannose and galactose. Fraction A had $[\alpha]_D^{17}$ +212° (*c* 0·40 in H_2O). An alkaline copper-complex of Fraction A was then fractionally precipitated with acetone. A gelatinous precipitate was rejected, and a flocculent precipitate collected, dissolved in water, acidified (acetic acid), and reprecipitated with acetone. The product, *iso*lichenin B, on acid hydrolysis gave glucose and no other sugar. An aqueous solution of *iso*lichenin B was dialysed for 2—3 days, passed through basic and acidic ion-exchange resins, and finally precipitated with alcohol (yield 1·9 g.).

In a second series of extractions, 0·8 g. of *iso*lichenin was obtained from 2 kg. of moss.

Examination of iso*Lichenin*.—The *iso*lichenin precipitate was a white fibrous solid. Hydrolysis with 0·5N-hydrochloric acid at 100° for 3—4 hr. gave glucose (96%) and no other sugar (quantitative paper chromatography [20]). No uronic acid could be detected in the polysaccharide (naphtharesorcinol test) or on paper chromatography of the acid hydrolysate. *iso*Lichenin had $[\alpha]_D^{15}$ +255° (*c* 1·0 in H_2O), contained 0·32% of ash and had a low reducing power towards hypoiodite with an apparent D.P. of 34. An aqueous solution was stained greenish-blue with iodine, the absorption spectrum having a maximum at 600 mμ, and a blue-value [19] of 0·01.

Periodate Oxidation of iso*Lichenin*.—The polysaccharide (99·6 mg.) was oxidised with potassium metaperiodate at room temperature, under the conditions described previously.[19,21] The formic acid production was as follows :

Time of oxidation (hr.)	24	48	96	144	168	192
Moles formic acid per $C_6H_{10}O_5$ residue, × 10^2	3·8	4·7	5·7	6·1	6·7	6·9

On the assumption that each molecule of *iso*lichenin gives rise to 3 moles of formic acid, the observed yield of formic acid corresponds to a chain length of about 42 units.

In a second experiment, *iso*lichenin (115·4 mg.) was oxidised with sodium metaperiodate (0·25M; 50 ml.). The periodate uptake was determined, at intervals, by Fleury and Lange's method : [22]

Time of oxidation (hr.)	24	48	72	96
Moles of periodate consumed per anhydroglucose unit	0·40	0·41	0·41	0·42

*iso*Lichenin therefore contains about 60% of periodate-resistant glucose residues.

Acetylation of iso*Lichenin*.—*iso*Lichenin (1·8 g.) was acetylated by Pacsu and Mullen's method [23] giving a chloroform- and acetone-soluble acetate (3·0 g.) [Found : CH_3·CO, 43·8. Calc. for $(C_{12}H_{16}O_8)_n$: CH_3·CO, 44·8%] with $[\alpha]_D^{16}$ +160° (*c* 1·04 in $CHCl_3$) and γ_{isp}^{20}/c 0·02254

[20] Flood, Hirst, and Jones, *J.*, 1948, 1679.
[21] Halsall, Hirst, and Jones, *J.*, 1947, 1399.
[22] Fleury and Lange, *J. Pharm. Chim.*, 1933, **17**, 107.
[23] Pacsu and Mullen, *J. Amer. Chem. Soc.*, 1941, **63**, 1487.

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(*c* 1·035 in $CHCl_3$) corresponding to an apparent D.P. of *ca.* 43, on the assumption that $Km = 5{\cdot}3 \times 10^{-4}$.[24]

Methylation of iso*Lichenin.*—*iso*Lichenin *O*-acetate (2·7 g.) in acetone solution was methylated four times with dimethyl sulphate and sodium hydroxide solution, and three times with methyl iodide and silver oxide. The partly methylated polysaccharide (OMe, 43·3%) was isolated and then fractionated by the solution method, with successive mixtures of chloroform and light petroleum (b. p. 65—70°), as follows :

Fraction	Petroleum–chloroform	Yield (g.)	OMe (%)
1	95 : 5	—	—
2	90 : 10	0·056	—
3	85 : 15	1·398	43·6
4	80 : 20	0·661	42·2

Fractions 3 and 4 were combined, and methylated by Freudenberg and Boppel's liquid-ammonia method.[25] At the end of the reaction, the neutralised mixture was extracted with chloroform, and the extract filtered, dried, and concentrated. Methylated *iso*lichenin was obtained as a white flocculent precipitate on pouring the concentrated solution into light petroleum (b. p. 40—60°) (Found : Ash, 0·5; OMe, 44·3. Calc. for tri-*O*-methylglucan, OMe, 45·6%). The methylated polysaccharide was then fractionated by the solution method, with chloroform–light petroleum (b. p. 70—80°) as follows :

Fraction	Petroleum–chloroform	Yield (g.)	η_{sp}/c (in $CHCl_3$)	$[\alpha]_D^{14}$ (in $CHCl_3$)	OMe (%)
1	90 : 10	0·036	—	—	—
2	85 : 15	1·42	0·0137	+218°	44·5
3	80 : 20	0·34	0·0184	+216	44·1

Fractions 2 and 3 were combined (Found : OMe, 44·4%).

Hydrolysis of Methylated iso*Lichenin and Separation of Methylated Sugars.*—An acid hydrolysate of a sample (10 mg.) was examined by paper chromatography. 2 : 3 : 4 : 6-Tetra- (R_G 1·00), 2 : 4 : 6-tri- (R_G 0·76), 2 : 3 : 6-tri- (R_G 0·83), and di-*O*-methylglucose were present.

Methylated *iso*lichenin (1·40 g.) was hydrolysed with (1%) methanolic hydrogen chloride (100 ml.) under reflux for 13 hr. (constant rotation). After neutralisation (diazomethane), the hydrolysate was concentrated, and further hydrolysed with boiling 0·5N-hydrochloric acid (100 ml.) for 10 hr. The neutralised and concentrated hydrolysate was extracted with chloroform, and this extract concentrated. The syrup (1·50 g.) was fractionated on a cellulose column[26] (70 × 2 cm.), light petroleum (b. p. 100—120°)–butan-1-ol (6 : 4) saturated with water being used as solvent. Three fractions were isolated, which contained 1·40 g. of sugars (93% recovery). Elution of the column with water gave a fourth fraction (13 mg.) containing traces of mono-*O*-methylglucose and glucose, which was not examined further.

Fraction 1. The syrup (0·161 g.) contained tetra-*O*-methylglucose (18·0%, by hypoiodite oxidation) and methyl glucosides of tri-*O*-methylglucoses. It was rehydrolysed with 0·5N-hydrochloric acid (10 ml.), neutralised, and chromatographed on a second cellulose column, giving fraction 1*a* (19 mg.) and 1*b* (118 mg.). Fraction 1*a* was identified as 2 : 3 : 4 : 6-tetra-*O*-methyl-D-glucose. After three recrystallisations from light petroleum (b. p. 40—60°), it had m. p. 83—85°, $[\alpha]_D^{17}$ +84° (*c* 0·53 in H_2O). Fraction 1*b* was a mixture of sugars with the same R_G values as 2 : 3 : 6- and 2 : 4 : 6-tri-*O*-methylglucose.

Fraction 2. This fraction (1·205 g.) was a mixture of 2 : 4 : 6- (major component) and 2 : 3 : 6-tri-*O*-methylglucose (paper chromatography). It was 90·3% pure, by hypoiodite oxidation. 2 : 3 : 4- and 3 : 4 : 6-Tri-*O*-methylglucose were absent; the sugars gave a negative Weerman reaction. Part of the fraction (300 mg.) was rechromatographed three times on a cellulose column, giving fraction 2*a* (150 mg.) and 2*b* (50 mg.). Fraction 2*a* was pure 2 : 4 : 6-tri-*O*-methyl-D-glucose. After recrystallisation from ether, it had m. p. 120—122°, $[\alpha]_D^{18}$ +75° (equil.) (*c* 1·1 in H_2O) (Found : OMe, 41·1. Calc. for $C_9H_{18}O_6$: OMe, 41·9%). The corresponding 2 : 4 : 6-tri-*O*-methyl-*N*-phenyl-D-glucosylamine had m. p. 143—145°. Fraction 2*b* was identified as 2 : 3 : 6-tri-*O*-methyl-D-glucose. On recrystallisation from ether, it had m. p. 114—116°, $[\alpha]_D^{17}$ +67° (equil.) (*c* 0·6 in H_2O). The phenylhydrazide of the derived

[24] Staudinger and Reinecke, *Annalen*, 1938, **535**, 95.
[25] Freudenberg and Boppel, *Ber.*, 1938, **71**, 2505.
[26] Hough, Jones, and Wadman, *J.*, 1949, 2511.

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2 : 3 : 6-tri-*O*-methyl-D-gluconic acid had m. p. 145° (Found : OMe, 28·9. Calc. for $C_{15}H_{24}O_6N_2$: OMe, 28·4%).

Fraction 3. This material (40 mg.; 70% pure by hypoiodite oxidation) appeared to contain 2 : 3-di-*O*-methylglucose (21%) and other di-*O*-methylglucoses (79%) as indicated by quantitative paper chromatography.

The weights and mol. proportions of sugars were : tetra-*O*-methyl- (0·031 g.; 1 mol.), tri-*O*-methyl- (1·220 g.; 42 mol.) and di-*O*-methyl-glucoses (0·028 g.; 1 mol.). *iso*Lichenin is therefore unbranched, and contains one non-reducing terminal group per 44 glucose residues.

Action of β-Amylase on iso*Lichenin.*—β-Amylase was prepared from barley by the method of Preece and Shadaksharaswamy.[27] The following digest was prepared : *iso*lichenin (50 mg.), 0·04M-acetate buffer (pH 4·6; 2 ml.), β-amylase solution (0·1%; 0·5 ml.), and water (5 ml.). After 48 hours' incubation at 38°, chromatography failed to show the presence of reducing sugars. The iodine-staining power of the polysaccharide was unchanged. In similar digests containing soluble starch or a mixture of starch and *iso*lichenin, maltose was detected after only 15 minutes' incubation.

A sample of purified soya-bean β-amylase kindly supplied by Professor S. Peat, F.R.S., likewise failed to attack *iso*lichenin.

Lichenin

Isolation of Lichenin.—The material which was precipitated from the hot-water extract of Iceland moss (p. 1954) was freed from *iso*lichenin by repeated precipitations from hot water. Addition of Fehling's solution to an alkaline solution of the lichenin gave an insoluble copper complex; after regeneration (acetic acid), the lichenin was precipitated with acetone and dried (yield 3 g. from 500 g. of moss). The polysaccharide was finally shaken with water for 5—6 hr. and reprecipitated with acetone.

Examination of Lichenin.—The lichenin preparations were white powders, insoluble in cold water, and soluble in hot water, or alkali; they had $[\alpha]_D$ +8° to +10° (*c* 1·0 in N-sodium hydroxide). Paper chromatography of acid hydrolysates gave glucose and no other sugar. Sample I had a glucose content of 94% (by polarimetric determination and quantitative paper chromatography [20]), ash content 0·88%, and a slight reducing action towards alkaline hypoiodite (apparent D.P. 80—86). Sample II had a glucose content of 96% (by cuprimetric titration) and an ash content of 0·23%.

Periodate Oxidation of Lichenin.—(a) *Sodium metaperiodate.* Lichenin (60—70 mg.) was shaken, in the dark, with 0·22M-sodium metaperiodate solution (15 ml.) for periods up to 72 hr. The periodate-uptake was determined as before. After 24, 48, and 72 hours' oxidation, both sample I and II had reduced 0·7 mole of periodate per anhydroglucose residue. Approximately 30% of the glucose residues in lichenin are therefore resistant to periodate oxidation.

(b) *Preparation of* iso*nicotinhydrazide and thiosemicarbazide polymers.* Lichenin (sample II) was treated with sodium metaperiodate for 72 hr. at room temperature, and the periodate-oxidised lichenin then isolated, washed, and dried. 50 Mg. portions, dissolved in hot water (2·5 ml.), were cooled and mixed with *iso*nicotinhydrazide (85 mg.) or thiosemicarbazide (56 mg.) in water (5 ml.). The precipitated polymers were collected, washed and dried : *iso*nicotinhydrazide polymer (Found : N, 11·6, equiv. to 66% of α-glycol groups); thiosemicarbazide polymer (Found : N, 12·7, equiv. to 67% of α-glycol groups).

(c) *Partial hydrolysis of the polyalcohol.* Periodate-oxidised lichenin (Sample II; 40 mg.) was treated with potassium borohydride (25 mg.) in water (2 ml.) for 5 hr. The polyalcohol was precipitated with alcohol, then hydrolysed with 0·5N-sulphuric acid (4 ml.) at 100° for 1·5 hr., and the neutralised concentrated hydrolysate examined by paper chromatography. Glucose was the only sugar present. Under similar conditions, a partial hydrolysate of lichenin contained glucose, laminaribiose, cellobiose and higher oligosaccharides.

Acetylation of Lichenin.—Lichenin (Sample I; 2·5 g.) on acetylation (Pacsu and Mullen's method [22]) gave lichenin acetate (3·4 g.) (Found : ash content 0·5; $CH_3{\cdot}CO$, 44·0. Calc. for $(C_{12}H_{16}O_8)_n$: $CH_3{\cdot}CO$, 44·8%). The acetate (3·0 g.) was fractionated from chloroform solution with light petroleum (b. p. 40—60°), as follows :

Fraction	Yield (g.)	Acetyl (%)	$[\alpha]_D^{16}$ (*c* 1·0 in $CHCl_3$)
1	0·4	43·8	−30°
2	2·2	44·2	−34

[27] Preece and Shadaksharaswamy, *Biochem. J.*, 1949, **44**, 271.

Lichenin acetate (Fraction 2) was deacetylated (sodium methoxide), and the regenerated polysaccharide treated with sodium metaperiodate. 0·7 Mole of periodate per anhydroglucose unit was consumed.

Methylation of Lichenin.—Lichenin (Sample I, 6·0 g.) on methylation (seven treatments with dimethyl sulphate and sodium hydroxide) gave a product with OMe 40·8%. Fractionation, by the solution method, with dry benzene–light petroleum (b. p. 75—80°), gave the following fractions :

Fraction	Petroleum–benzene	Yield (g.)	OMe (%)	$[\alpha]_D^{17}$ (in $CHCl_3$)
1	95 : 5	0·08	41·5	−8·2°
2	90 : 10	2·13	43·9	−8·1
3	85 : 15	1·34	43·1	−7·9
4	80 : 20	0·10	39·8	—

Fractions 2 and 3 were combined, and treated twice with methyl iodide and silver oxide. The product had $[\alpha]_D^{17}$ −8·2° (*c* 0·74 in $CHCl_3$) (Found : ash content 0·81 ; OMe, 44·4%).

Hydrolysis of Methylated Lichenin and Separation of Methylated Sugars.—Paper chromatography of an acid hydrolysate of 10 mg. methylated lichenin showed the presence of 2 : 3 : 4 : 6-tetra- (R_G 1·00), 2 : 3 : 6-tri- (R_G 0·83), 2 : 4 : 6-tri- (R_G 0·76) and di-*O*-methylglucoses.

Methylated lichenin (3·0 g.) was hydrolysed successively with methanolic and aqueous hydrogen chloride, and the resulting syrup (3·2 g.) fractionated on a cellulose column [26] (90 × 2·5 cm.) as described previously.

Fraction	Yield (g.)	Components	Purity (%, by hypoiodite oxidation)
1	0·455	Tetra-*O*-methylglucose and methyl tri-*O*-methylglucosides	10·3
2	2·469	Tri-*O*-methylglucoses	91·5
3	0·039	Di-*O*-methylglucoses	85·1

A fourth fraction (15 mg.) was eluted from the column with water.

Fraction 1. Rehydrolysis and chromatography gave fraction 1*a* (32 mg.) and 1*b* (410 mg.). Fraction 1*a* crystallised, and was identified as 2 : 3 : 4 : 6-tetra-*O*-methyl-D-glucose ; after recrystallisation from light petroleum (b. p. 40—60°) it had m. p. 83—86°, $[\alpha]_D^{15}$ +83° (*c* 0·67 in H_2O). Fraction 1*b* was a mixture of tri-*O*-methylglucoses.

Fraction 2. Paper chromatography showed that 2 : 3 : 4-tri-*O*-methylglucose (R_G 0·85) was absent. The material gave a negative Weerman reaction, indicating the absence of the 3 : 4 : 6-isomer. Part of fraction 2 (500 mg.) was rechromatographed on cellulose columns ; fractions 2*a* (333 mg.), 2*b* (129 mg.), and 2*c* (18 mg.) were obtained. Fraction 2*a* was pure 2 : 3 : 6-tri-*O*-methyl-D-glucose. Recrystallisation from ether gave crystals, m. p. 120—122°, $[\alpha]_D^{16}$ +67° (equil.) (*c* 0·53 on H_2O) (Found : OMe, 40·9. Calc. for $C_9H_{18}O_6$: OMe, 41·9%). The phenylhydrazide of the derived aldonic acid had m. p. 145° (Found : N, 8·3 ; OMe, 27·7. Calc. for $C_{15}H_{24}O_6N_2$: N, 8·6 ; OMe, 28·4%). Fraction 2*b* was identified as 2 : 4 : 6-tri-*O*-methyl-D-glucose. After recrystallisation (dry ether), it had m. p. 119—123°, $[\alpha]_D^{17}$ +74° (equil.) (*c* 0·82 in H_2O) (Found : OMe, 40·5. Calc. for $C_9H_{18}O_6$: OMe, 41·9%). Treatment with aniline gave 2 : 4 : 6-tri-*O*-methyl-*N*-phenyl-D-glucosylamine with m. p. 143—144°. Fraction 2*c* was a mixture of tri-*O*-methylglucoses.

The rotation of the tri-*O*-methyl fraction in cold methanolic 2% hydrogen chloride was $[\alpha]_D$ +36° ⟶ −15° constant in 24 hr. (*c* 1·04). An authentic mixture of 2 : 3 : 6- (68%) and 2 : 4 : 6-tri-*O*-methyl-D-glucose (32%) showed $[\alpha]_D$ +57° ⟶ −13° constant in 24 hr. (*c* 1·08 in methanolic 2% hydrogen chloride).

Fraction 3. The syrup contained 2 : 3-di-*O*-methylglucose (53%) together with other di-*O*-methylglucoses (47%) by quantitative paper chromatography. In qualitative experiments, treatment of pure 2 : 4 : 6-tri- and 2 : 3 : 6-tri-*O*-methylglucose with N-hydrochloric acid at 100° for 3 hr. gave about 1% of mixed di-*O*-methylglucoses and a trace of mono-*O*-methylglucose. Fraction 3 is therefore considered to be due to (*a*) hydrolytic demethylation and (*b*) under-methylation.

Since 2·724 g. of methylated sugars contained 0·047 g. of pure tetra-*O*-methylglucose, lichenin has an average chain length of *ca.* 62 glucose residues.

Action of β-Glucosidase Preparations on Lichenin.—A fine suspension of lichenin was prepared either by dissolution in 0·2N-sodium hydroxide followed by neutralisation with hydrochloric acid (phenolphthalein) or by warming an aqueous suspension of lichenin to 50°. β-Glucosidase

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action was studied qualitatively by incubating a lichenin suspension (1%; 2 ml.), 0·2M-acetate buffer (pH 4·6 or 5·0; 0·5 ml.), and β-glucosidase solution (0·5 or 1·0 ml.) at 37°. Samples were analysed at intervals, by paper chromatography, using authentic specimens of glucose, laminaribiose, and cellobiose as reference compounds.

Type of β-glucosidase	Source of enzyme	Method of prep. ref.	Product(s)
Exo-	Almond emulsin	28	Glucose
Exo-	*Helix aspersa*	29	Glucose
Endo-	Malted barley	30	Glucose, cellobiose, laminaribiose and higher oligosaccharides
Endo-	*Cladophora rupestris*	15	Glucose, cellobiose, laminaribiose and higher oligosaccharides.

In a further experiment, lichenin suspension (3 mg./ml.; 5 ml.), 0·2M-acetate buffer (pH 5·0; 2 ml.), and almond β-glucosidase [28] (10 mg. in water; 1 ml.) were incubated at 35°. After 3 days, 12% conversion into glucose was observed (Shaffer–Somogyi estimation). In a control experiment, laminarin $\{[\alpha]_D +9°$ (c 2·7 in N-NaOH)$\}$ gave 15% conversion into glucose.

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Department of Chemistry, University of Edinburgh. [*Received, December 27th*, 1956.]

[28] Neuberg and Hassid, *Arch. Biochem. and Biophys.*, 1955, **59**, 405.
[29] Karrer, Staub, Weinhagen, and Joos, *Helv. Chim. Acta*, 1924, **7**, 144.
[30] Euler and Svanberg, *Z. physiol. Chem.*, 1921, **112**, 193; Pringsheim and Leibowitz, *ibid.*, 1923, **131**, 262.

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376. *Aspects of Stereochemistry. Part I. Stereospecificity in Formation of Epoxides from Cyclic Allylic Alcohols.*

By H. B. Henbest and R. A. L. Wilson.

Formation of epoxides from cyclic allylic alcohols occurs on the side *cis* to the hydroxyl group. Study of reaction velocities confirms that the hydroxyl group exerts a promoting effect, and the hypothesis of a hydrogen-bonded transition state is advanced in explanation.

A paper-chromatographic technique for the separation of *cyclo*hexanediols is discussed.

With certain exceptions, notably those derived from the concept of conformational analysis,[1] the factors governing the selective formation of geometrical isomers in cyclic systems are inadequately understood. In studies to shed light on the stereochemical pathways followed in the reactions of alicyclic compounds, the stereochemistry of epoxide formation from monosubstituted *cyclo*hexenes and organic per-acids has been investigated first. The present paper is concerned with allylic systems.

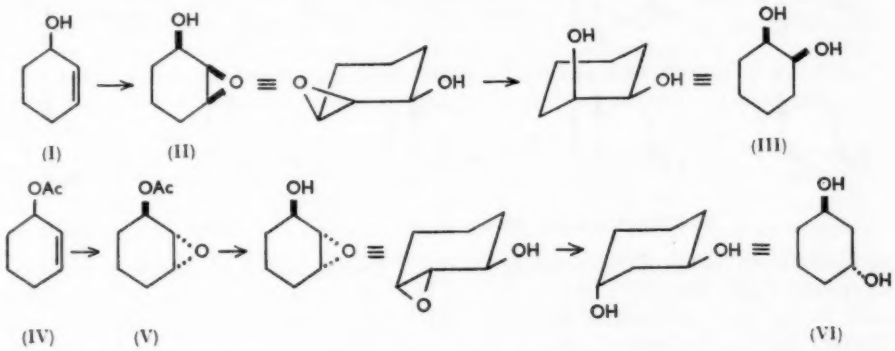
Variation of functional group at the position allylic to a double bond is most conveniently achieved with *cyclo*hex-2-enol (I) and related compounds. Formation of an epoxide from the alcohol (I) has been described by Kotz and Richter,[2] but the homogeneity and/or geometrical configuration of the product were not determined.

The epoxide has now been shown to be homogeneous by distillation into fractions with identical refractive index and infrared absorption, and by the formation of a 3 : 5-dinitrobenzoate in 90% yield. A *cis*-relation of the epoxy- and the hydroxy-group (*i.e.*, II) was proved by reduction by lithium aluminium hydride to *cyclo*hexane-*cis*-1 : 2-diol (III). Although this diol was only isolated in 60% yield, its formation in about 90% yield was indicated by periodate titration (92% of 1 : 2-diol) and by paper chromatography (see below), which gave no indication of the presence of the *trans*-1 : 2-diol. If, in the reduction

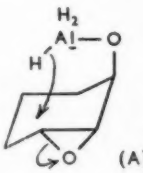
[1] Cf. Barton and Cookson, *Quart. Rev.*, 1956, **10**, 44.
[2] Kotz and Richter, *J. prakt. Chem.*, 1925, **111**, 373.

of the epoxide (II) by lithium aluminium hydride, the hydroxyl group (or derived metal complex) is equatorial to the distorted chair conformaton [3] scission of the epoxide to give the 1 : 2-diol follows the general rule whereby axial substituents are formed.

The epoxidation of 3-acetoxy*cyclo*hex-1-ene (IV) was slower than that of (I). Fractionation of the product indicated nonhomogeneity and a crystalline 3 : 5-dinitrobenzoate was not obtained from the hydrolysed material. However, it seems that the major



component of the mixture is the isomer with the epoxide group *trans* to the acetate group (*i.e.*, V). Thus, alkaline hydrolysis of the epoxy-acetate (V) gave an epoxy-alcohol [infrared spectrum different in detail from that of (II)] which on reduction by lithium aluminium hydride afforded diol containing only 19% of the 1 : 2-isomer, the greater part therefore being the 1 : 3-diol. Paper chromatography of this mixture of diols confirmed the presence of the 1 : 3-isomer, and showed that the 1 : 2-diol consisted of a mixture of the *cis*- and *trans*-compounds. Since the pure *cis*-epoxy-alcohol (II) yields 90% of 1 : 2-diol on reduction, the results indicate that the *trans* : *cis* ratio in the epoxide from the acetate (IV) is approximately 4 : 1. The predominant formation of the 1 : 3-diol (VI) on reduction of the *trans*-epoxy-alcohol is again in accord with conformational expectation if the original hydroxyl group (or derived metal complex) is equatorial; the production of a small amount of the *trans*-1 : 2-diol may be explained by the occurrence of some intramolecular attack by hydride employing the alternative conformation shown in (A) inset. A more detailed discussion of the reduction by hydride of other epoxy-alcohols proceeding by an intramolecular mechanism will be presented later.



(A)

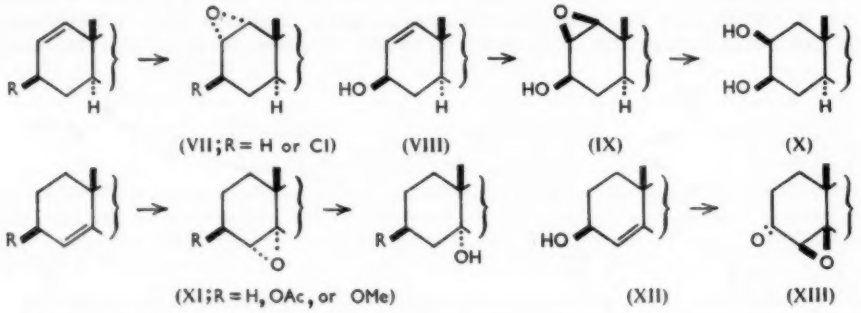
Knowledge of stereochemistry of steroids and availability of a variety of allylic alcohols prompted investigation of these reactions in the steroid series. The relatively bulky angular methyl groups on the front (β) side of the molecule cause most reagents to approach from the rear (α).[4] In this connection, peracid reactions are particularly stereospecific, high yields of α-epoxides usually being obtained from olefins if (*a*) the ring system, considered as a whole, is relatively flat with the 5α : 8β : 9α : 10β : 14α-configuration (" 5-*allo*-series ") wherever possible, and (*b*) additional bulky groups of α-configuration are not close to the olefinic bond.

Thus cholest-1-ene and 3β-chlorocholest-1-ene afford α-epoxides (VII) in good yields.[5] In contrast, 3β-hydroxycholest-1-ene (VIII) affords the β-epoxide (IX) the structure being established by reduction with hydride to cholestane-2β : 3β-diol (X) [6] (*iso*propylidene derivative readily formed).

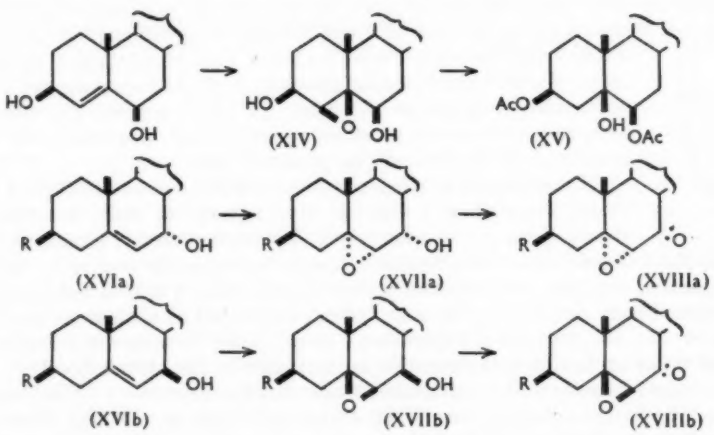
[3] Ottar, *Acta Chem. Scand.*, 1947, **1**, 283.
[4] Fieser, *Experientia*, 1950, **6**, 312.
[5] Henbest and Wilson, *J.*, 1956, 3289.
[6] Henbest and Smith, *J.*, 1957, 926.

XUM

Cholest-4-ene and 3β-acetoxy- and 3β-methoxy-cholest-4-enes all give high yields of α-epoxides (XI), the structures of the products being established by reduction with hydride to 5α-hydroxy-compounds. For comparison, the new 3β-methoxy-5α-alcohol was prepared



by partial methylation of the known 3β : 5α-diol. Epoxidation of the related 3β-hydroxy-compound (XII) afforded a non-crystalline product which on chromic acid oxidation gave the known coprostanone derivative (XIII), thus confirming β-epoxide formation. Plattner and his co-workers [7] showed that epoxidation of the mixture of 3α- and 3β-alcohols (mainly the latter), obtained by lithium aluminium hydride reduction of cholest-4-en-3-one, followed by acetylation and chromatography, afforded the 3β-acetoxy-4β : 5β-epoxide (45%) and the 3β-acetoxy-4α : 5α-epoxide (5%) (both from the original 3β-alcohol) together with the 3α-acetoxy-4α : 5α-epoxide (11%) (from the original 3α-alcohol). The detection in this experiment of a small amount of α-epoxide formed from a β-alcohol indicates that the shielding effect of the angular methyl group is operating to some extent (see below, rates of epoxidation of 7-hydroxy-Δ^5-compounds). Even stronger shielding would be expected in ring C of the steroid nucleus, and the formation of a β-epoxide from a 12β-hydroxy-Δ^9-compound would probably be much inhibited.



cis-Epoxidation being assumed, the 4 : 5-epoxide first prepared by Rosenheim and Starling [8] from 3β : 6β-dihydroxycholest-4-ene should have the 4β : 5β-configuration (XIV), and this was confirmed by its reduction with lithium aluminium hydride to a triol yielding

[7] Plattner, Heusser, and Kulkarni, *Helv. Chim. Acta*, 1949, **32**, 1070.
[8] Rosenheim and Starling, *J.*, 1937, 377.

a new diacetoxy-alcohol (XV) on acetylation. The presence of a *cis*-3 : 5-alcohol-ester grouping in (XV) was also indicated by the characteristic chelation shown in the infrared absorption spectrum (see following paper).

Two further examples of the stereospecific epoxidation were provided by the reactions of the epimeric 7-hydroxycholesteryl benzoates (XVIa and b) with perbenzoic acid. The two epoxides obtained as the major products from the reactions were each oxidised by chromic acid–acetone [9] to yield different epoxy-ketones. The configurations of the epoxide groups are thus different, and in view of the previous results and the epoxidation rates (see below) it is considered that each initial product isolated is a *cis*-epoxy-alcohol (XVIIa and b) and that the derived ketones are (XVIIIa and b). It may be noted that peracid oxidation of the related deoxy-compound, cholesteryl benzoate, is known to give a mixture of α- and β-epoxides.[10]

The results therefore show that allylic alcohols direct attack specifically at the *cis*-side even in steroids where β-approach of reagents is normally difficult. In order to study the effect in further detail the velocities of some of the above reactions have been measured. The olefin–peracid reaction is known to be of first order with respect to each reactant, and the electrophilic character of the reagent attacking the double bond may be inferred from the fact that electron-attracting groups near the unsaturated bond reduce the reaction velocity whereas increasing alkylation of the olefin increases the rate.[11] The rates (see Table) were determined in benzene solution at 5°, perbenzoic acid being the oxidant.

The monocyclic compounds being considered first, it can be seen that introduction of the various oxygen substituents causes a reduction in rate in accord with their inductive (electron-attracting [12]) properties. However, the most striking feature is that the alcohol reacts about eight times more rapidly than the corresponding methyl and ethyl ethers, for the relative inductive strengths of these groups would not be expected to be very

Oxidation of cyclo*hexenes with perbenzoic acid at* 5°.

	10^4k (mole^{-1} l. sec.$^{-1}$)	Relative rate
*cyclo*Hexene	63·3	1·0
3-Hydroxy*cyclo*hexene	34·5	0·55
3-Methoxy*cyclo*hexene	4·25	0·067
3-Ethoxy*cyclo*hexene	4·72	0·075
3-Acetoxy*cyclo*hexene	2·90	0·046
4-Hydroxy*cyclo*hexene	2·67	0·42
Cholesteryl benzoate	229	3·6
7α-Hydroxycholesteryl benzoate	124	1·8
7β-Hydroxycholesteryl benzoate	56	0·88

different.[13] The similarity of the rates of the two ethers indicates that steric factors are not likely adequately to explain the difference in rate between alcohol and ether. Another significant observation is that the βγ-unsaturated alcohol, *cyclo*hex-3-en-1-ol, reacts more slowly than its allylic isomer (I), although in the former the hydroxyl group is more remote from the double bond. Thus the allylic alcohol is exceptional in reacting more rapidly than expected. The hydroxyl group is clearly exerting some promoting effect which in turn may be correlated with its directive influence in giving *cis*-epoxy-alcohols. The rate studies and the stereochemical results may be accommodated by postulating that hydrogen bonding causes an association of the reactants favourable for interaction between the electrophilic peracid oxygen and the olefin; a suggested transition complex is (B).

The rates of epoxidation of the steroids may be explained in similar terms, although

[9] Bladon, Fabian, Henbest, Koch, and Wood, *J.*, 1951, 2402.
[10] Baxter and Spring, *J.*, 1943, 613.
[11] Swern, *Chem. Rev.*, 1949, **45**, 1.
[12] In the present context, the term " inductive " applied to oxygenated groups embraces all types of electron attraction towards oxygen, cf. Roberts and Carboni, *J. Amer. Chem. Soc.*, 1955, **77**, 5554.
[13] Taft, *ibid.*, 1953, **75**, 4236.

XUM

the intrusion of steric factors at times becomes apparent. Cholesteryl benzoate reacts about twice as fast as its 7α-hydroxy-derivative—a rate difference very similar to that between *cyclo*hexene and *cyclo*hex-2-en-1-ol. However, a further reduction in rate is

(B)

observed with the 7β-hydroxy-compound, which may be ascribed to the operation of the usual shielding effect of the angular methyl groups on the β-face. Nevertheless the predominant formation of the β-epoxide shows that the β-approach of reagent encouraged by the hydroxyl group is more favoured than approach from the less hindered α-face. The hypothetical relative rate for reaction at the α-face is calculated to be very approximately 0·32 (cholesteryl benzoate relative rate × 0·07; the inductive effect of hydroxyl being assumed to be the same as that of alkoxyl in the simpler series), appreciably less than the observed relative rate of 0·88 (mainly representing β-approach).

Paper Chromatography of cyclo*Hexanediols.*—Although individually the six *cyclo*hexanediols crystallise well, the isolation by conventional methods of one isomer from reaction products containing related polar compounds is often attended with such losses as to make an estimation of yield difficult and the detection of minor amounts of associated isomers almost impossible. The chromatographic separation of the 1 : 2- and 1 : 3-diols on paper has therefore been explored, methods being employed based on the observations by Partridge [14] and by Hough [15] concerning the detection of polyhydric alcohols on paper (the authors thank Dr. D. C. C. Smith of this Department for drawing their attention to these possibilities). The results show that characteristic R_F differences between the *cis*- and the *trans*-1 : 2-diols and the two 1 : 3-diols (R_F values of *cis*- and *trans*-compounds very similar) enable some separation and detection of small amounts of these isomers to be achieved.

Experimental

M. p.s were determined on a Kofler hot stage. Optical rotations were measured in chloroform solutions. The infrared spectra of all compounds prepared were consistent with the structures assigned.

cis-2 : 3-*Epoxy*cyclo*hexanol* (II).—Solutions of *cyclo*hex-2-en-1-ol (12 g.) in benzene (200 c.c.) and perbenzoic acid (0·42M-solution; 290 c.c.) were cooled to 0°, mixed, and kept at 0°. At intervals aliquot portions were titrated to determine the concentration of remaining peracid. After 2·5 hr. the solution was washed with aqueous potassium carbonate and dried, and the solvent removed under reduced pressure. Distillation (short-path) gave the *epoxide* (1·8 g.), b. p. 100°/12 mm., n_D^{18} 1·4867 (Found : C, 63·0; H, 8·7. $C_6H_{10}O_2$ requires C, 63·1; H, 8·8%) The homogeneity of the product was demonstrated by distillation into four fractions of identical refractive index and infrared absorption.

The low yield results from the isolation technique; an improved method (80% yield) of preparing the epoxide has since been evolved (to be published with Mr. B. Nicholls).

A solution of the epoxy-alcohol (0·2 g.) and 3 : 5-dinitrobenzoyl chloride (0·44 g.) in benzene (10 c.c.) and pyridine (0·2 c.c.) was kept at 20° for 2 hr. The 3 : 5-*dinitrobenzoate* (0·5 g.) crystallised from methanol as plates, m. p. 112—114·5° (Found : C, 51·0; H, 3·9; N, 9·3. $C_{13}H_{12}O_7N_2$ requires C, 50·7; H, 3·9; N, 9·1%).

[14] Partridge, *Nature*, 1946, **158**, 270.
[15] Hough, *ibid.*, 1950, **165**, 400.

Epoxidation of 3-*Acetoxy*cyclo*hex*-1-*ene* (IV).—Solutions of the acetate (12 g.) in benzene (200 c.c.) and perbenzoic acid in benzene (0·48M-solution; 200 c.c.) were cooled to 0° and mixed. Aliquot portions were removed periodically from the reaction solution kept at 0° in order to follow the rate of consumption of the peracid. After 31 hr. the solution was washed with saturated potassium carbonate solution twice and dried and the solvent removed under reduced pressure. Distillation of the residue (6 g.) gave three fractions: (1) b. p. 94—110°/14 mm., n_D^{20} 1·4610; (2) b. p. 110—116°/14 mm., n_D^{20} 1·4615; (3) b. p. 116—117°/14 mm., n_D^{20} 1·4632. The infrared spectra of these fractions were very similar but not quite identical; the absence of starting material from each was indicated by the non-appearance of the olefinic CH bending bands at 710 and 727 cm.$^{-1}$. The fractions were combined (Found: C, 61·2; H, 8·0. Calc. for $C_8H_{12}O_3$: C, 61·5; H, 7·8%) for the reduction (below).

Reductions with Lithium Aluminium Hydride.—(*a*) A solution of *cis*-2 : 3-epoxy*cyclo*hexanol (0·7 g.) and lithium aluminium hydride (0·3 g.) in ether (20 c.c.) was heated under reflux for 3 hr. Ethyl acetate (100 c.c.) was added, cautiously at first, followed by dilute sulphuric acid. The ethyl acetate layer was then washed with saturated potassium carbonate and sodium chloride solutions and dried. Removal of solvent under reduced pressure and crystallisation from ethyl acetate gave *cyclo*hexane-*cis*-1 : 2-diol (0·4 g.), m. p. and mixed m. p. with an authentic sample 94—96°.

Periodate titration indicated that the crude diol contained 92% of 1 : 2-diol.

(*b*) Solutions of 3-acetoxy-1 : 2-epoxy*cyclo*hexane (2 g.) in methanol (20 c.c.) and potassium hydroxide (1 g.) in water (20 c.c.) were mixed and kept overnight at 20°. The epoxy-alcohol was isolated with ether: its infrared spectrum was similar to but not identical with that of the *cis*-epoxy-alcohol; only a trace of acetate remained. The epoxy-alcohol in ether (50 c.c.) was then heated under reflux with lithium aluminium hydride (0·5 g.) for 2 hr. The diol was isolated with ethyl acetate as before.

Periodate titration indicated that the crude diol contained 19% of 1 : 2-diol.

Paper Chromatographic Separation of Diols.—The methods of Partridge and of Hough were modified as follows. The mobile phase consisted of the upper layer obtained by shaking together equal volumes of water, xylene, and ethyl methyl ketone, and the lower layer was placed in the tank. Part of the upper phase was also exposed separately in the tank for equilibration. After development the paper was dried at 20°, sprayed with ammoniacal silver nitrate solution, again allowed to dry, and then kept in an oven at 100° until the contrast between the brownish-black spot(s) and the paler brown background was suitable for visual inspection and photographic recording. This operation is desirable as the background colour slowly darkens. No attempt was made to put the method on to a quantitative basis although this should be possible. For equal amounts of substance, the 1 : 2-diols give much darker spots than the 1 : 3-diols.

Chromatography of the crude diol from the *cis*-epoxy-alcohol (II) gave only one spot, corresponding to *cyclo*hexane-*cis*-1 : 2-diol. Chromatography of the crude diol from the hydrolysed epoxy-acetate mixture gave three spots, corresponding to 1 : 3-diol (the R_F difference

R_F values of cyclo*hexanediols.*

cis-1 : 2-Diol	0·38	*cis*-1 : 3-Diol	0·07
trans-1 : 2-Diol	0·25	*trans*-1 : 3-Diol	0·06

between the *cis*- and the *trans*-compound is not great enough to make identification certain) and both 1 : 2-diols.

Epoxidation of 3β-*Hydroxychoiest*-1-*ene* (VIII).—The steroid (0·5 g.) in ether (50 c.c.) and monoperphthalic acid (1·9N-solution in ether; 8·6 c.c.) were kept at 20° for 6 days. The steroid was isolated with ether and chromatographed on alumina (20 g.) to give starting material (70 mg.) and the 1β : 2β-*epoxide* (IX) (0·24 g.), 172—175° (after crystallisation from acetone), $[\alpha]_D$ +63° (Found: C, 80·5; H, 11·6. $C_{27}H_{46}O_2$ requires C, 80·6; H, 11·5%). Acetylation afforded 3β-*acetoxy*-1β : 2β-*epoxycholestane*, m. p. 111—113°, $[\alpha]_D$ +66° (Found: C, 78·5; H, 10·7. $C_{29}H_{48}O_3$ requires C, 78·3; H, 10·9%).

The epoxy-alcohol (IX) (0·4 g.) was reduced with lithium aluminium hydride (0·2 g.) in ether (100 c.c.), at 20° for 16 hr. After the addition of ethyl acetate and dilute sulphuric acid, the steroid was isolated with ether and crystallised from ethyl acetate–methanol, giving cholestane-2β : 3β-diol (X) (0·33 g.) as fine needles, m. p. and mixed m. p. 173—176°, $[\alpha]_D$ +39°. This diol has been prepared previously from cholest-2-ene.[6]

XUM

A solution of the diol (0·1 g.) in acetone (50 c.c.) containing anhydrous copper sulphate (0·25 g.) was kept at 20° for 14 days. The *isopropylidene derivative* formed needles (from acetone), m. p. 114—117°, $[\alpha]_D$ +40° (Found: C, 81·0; H, 12·0. $C_{30}H_{52}O_2$ requires C, 81·0; H, 11·8%). Infrared spectrum (in CS_2): strong peak at 1052 cm.$^{-1}$ characteristic of *iso*propylidene derivatives, no hydroxyl bands. The *iso*propylidene derivatives of 3β : 4β-dihydroxycholest-5-ene and its 5α : 6α-epoxide both give strong peaks at 1060 cm.$^{-1}$.

Epoxidation of 3β-*Hydroxycholest-4-ene* (XII).—Solutions of the steroid (0·33 g.) in benzene (50 c.c.) and perbenzoic acid in benzene (0·41M; 6 c.c.) were mixed at 0° and then kept at 20° for 18 hr. After isolation with benzene, the product, in acetone (50 c.c.), was oxidised with chromic acid.[9] The ketone was isolated with ether and chromatographed on alumina (25 g.). Elution with benzene (150 c.c.) yielded 4β : 5β-epoxycoprostan-3-one (XIII) (0·24 g.), m. p. 115—118° (from methanol). Identity with an authentic sample was confirmed by mixed m. p. and by comparison of infrared spectra.

Epoxidation of 3β-*Methoxycholest-4-ene*.—The starting material was conveniently prepared by dissolving 3β-hydroxycholest-4-ene (0·3 g.) in a solution of potassium *tert.*-butoxide (M; 7·8 c.c.) and adding methyl iodide (0·5 c.c.). The solution was kept for 1 hr. at 20°, and the methoxy-steroid was then isolated with ether, forming plates (from acetone) (0·21 g.), m. p. 71·5—73°, $[\alpha]_D$ +36·5°. Evans and Shoppee [16] record m. p. 68—70°, $[\alpha]_D$ −37° (sign should be positive).

Solutions of the methoxy-steroid (0·3 g.) in benzene (25 c.c.) and perbenzoic acid in benzene (0·45M; 3·4 c.c.) were mixed at 0°, and then kept at 20° for 18 hr. A light petroleum solution of the product was filtered through alumina (20 g.) to give the α-*epoxide* (XI; R = MeO) (0·27 g.) (from acetone), m. p. 58—59°, $[\alpha]_D$ +57° (Found: C, 80·6; H, 11·5. $C_{28}H_{48}O_2$ requires C, 80·7; H, 11·6%).

3β-*Methoxycholestan-5α-ol*.—(*a*) A solution of 4α : 5α-epoxy-3β-methoxycholestane (0·1 g.) and lithium aluminium hydride (50 mg.) in ether (50 c.c.) was heated under reflux for 4 hr. The 5α-alcohol (80 mg.), needles (from acetone), m. p. 133—136°, $[\alpha]_D$ +23°, was identical (mixed m. p. and infrared spectrum) with a sample prepared by method (*b*).

(*b*) Methyl iodide (0·7 c.c.) was added to previously mixed solutions of 3β : 5α-dihydroxycholestane (0·4 g.) in *tert.*-butyl alcohol (10 c.c.) and potassium *tert.*-butoxide in *tert.*-butyl alcohol (M, 10 c.c.) and the mixture was kept at 20° for 1·5 hr. The product, isolated with ether, was chromatographed on alumina (20 g.). Elution with benzene–ether (3 : 2; 150 c.c.) yielded 3β-*methoxycholestan-5α-ol* (0·1 g.), m. p. 133—136° (from acetone), $[\alpha]_D$ +22° (Found: C, 80·3; H, 11·9. $C_{28}H_{50}O_2$ requires C, 80·3; H, 12·0%). Further elution with ether gave starting material (0·3 g.).

Epoxidation of 3β-*Acetoxycholest-4-ene*.—Solutions of the steroid (0·21 g.) in benzene (25 c.c.) and perbenzoic acid (0·45M; 2·5 c.c.) were mixed and kept at 20° for 18 hr. 3β-Acetoxy-4α : 5α-epoxycholestane (XI; R = AcO) (0·17 g.) was obtained as plates (from methanol), m. p. 117—119°, $[\alpha]_D$ +60° (Found: C, 78·3; H, 11·0. Calc. for $C_{29}H_{48}O_3$: C, 78·3; H, 10·9%). Plattner *et al.*[6] record m. p. 116—117°, $[\alpha]_D$ +67°, for this compound.

This epoxide (50 mg.) and lithium aluminium hydride (40 mg.) in ether (40 c.c.) were heated under reflux for 2 hr. The product was 3β : 5α-dihydroxycholestane (40 mg.) (from methanol), m. p. and mixed m. p. 224—227°.

4β : 5β-*Epoxycholestane*-3β : 6β-*diol* (XIV).—To a partial solution of powdered 3β : 6β-dihydroxycholest-4-ene (1 g.) in chloroform (50 c.c.) perbenzoic acid (0·48M solution in benzene; 10 c.c.) was added and the mixture was kept at 20°. After 7 hr. the solution was washed with aqueous sodium carbonate solution, passed through alumina (10 g.), and evaporated under reduced pressure. Recrystallisation from acetone afforded the epoxide (0·75 g.) as needles, m. p. 161—164°. Rosenheim and Starling [7] record m. p. 164—165°.

A solution of the epoxide (0·65 g.) and lithium aluminium hydride (0·5 g.) in dry tetrahydrofuran (25 c.c.) was heated under reflux for 2 hr. The steroid was isolated with ether, acetylated, and chromatographed on deactivated alumina (50 g.). The fractions obtained by elution with light petroleum (b. p. 60—80°)–benzene (3 : 1) gave 3β : 6β-*diacetoxycoprostan*-5β-*ol* (XV) (0·28 g.) as laths (from methanol), m. p. 165—167°, $[\alpha]_D$ +16° (Found: C, 73·4; H, 10·4. $C_{31}H_{52}O_5$ requires C, 73·75; H, 10·4%). A mixture with 3β : 6β-diacetoxycholestan-5α-ol (m. p. 165°) had m. p. 140—145°.

Epoxidation of 7α-*Hydroxycholesteryl Benzoate* (XVIa).—Solutions of the steroid (0·15 g.) in

[16] Evans and Shoppee, *J.*, 1953, 540.

benzene (10 c.c.) and perbenzoic acid in benzene (0·4M; 1·8 c.c.) were mixed and kept at 20° for 16 hr. Isolation with ether followed by crystallisation from acetone gave the 5α : 6α-*epoxide* (XVIIa) (0·125 g.) as needles, m. p. 191—193°; $[\alpha]_D$ −52° (Found: C, 78·1; H, 9·9. $C_{34}H_{50}O_4$ requires C, 78·1; H, 9·6%). Oxidation of this compound (0·1 g.) in acetone (25 c.c.) with a slight excess of chromic acid • afforded 3β-*benzoyloxy*-5α : 6α-*epoxycholestan*-7-*one* (XVIIIa) (needles from acetone), m. p. 178—182°, $[\alpha]_D$ −23° (Found: C, 78·8; H, 9·3. $C_{34}H_{48}O_4$ requires C, 78·4; H, 9·3%).

Epoxidation of 7β-*Hydroxycholesteryl Benzoate* (XVIb).—Solutions of the steroid (1 g.) in benzene (50 c.c.) and perbenzoic acid in benzene (0·4M; 12 c.c.) were mixed and kept at 20° for 16 hr. After isolation with ether the steroid was chromatographed on alumina (50 g.). Elution with benzene–ether (4 : 1) and crystallisation from acetone yielded the 5β : 6β-*epoxide* (XVIIb) (0·71 g.) as prisms, m. p. 173—177° remelting at 185—186°, $[\alpha]_D$ +46° (Found: C, 78·0; H, 9·9. $C_{34}H_{50}O_4$ requires C, 78·1; H, 9·6%). A solution of this alcohol (0·3 g.) in acetone (50 c.c.) was oxidised with chromic acid; 3β-*benzoyloxy*-5β : 6β-*epoxycholestan*-7-*one* (XVIIIb) formed plates (from acetone), m. p. 156—158°, $[\alpha]_D$ +24° (Found: C, 78·2; H, 9·2%).

The authors of this and the following papers thank Professor E. R. H. Jones, F.R.S., for his help and encouragement, Dr. G. D. Meakins for infrared spectra, and Mr. E. S. Morton for microanalyses. They also thank Dr. L. N. Owen (Imperial College) for samples of *cyclo*hexane-1 : 3-diols (this paper), and the Department of Scientific and Industrial Research for a Maintenance Grant (to R. A. L. W.).

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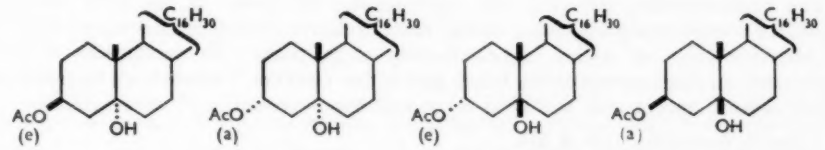
377. *Aspects of Stereochemistry. Part II.* Intramolecular Electrophilic Assistance of Displacement Reactions.*

By H. B. HENBEST and (MISS) B. J. LOVELL.

If, in a monoester of a 1 : 3-diol, the hydroxyl and ester groups are held close together by their molecular environment, hydrogen bonding to the *alcohol* oxygen of the ester occurs. Such hydrogen bonding facilitates hydrolysis of the ester, and in *cyclo*hexane compounds the usual rule whereby equatorial esters are more easily hydrolysed than axial esters can be reversed. The rôle of the neighbouring hydroxyl group in these reactions may be regarded as that of an intramolecular electrophil.

WITH the intention of finding suitable conditions for selective hydrolyses of 3-acetoxy-5-hydroxy-steroids, aqueous potassium hydrogen carbonate was studied, and conditions were thereby found under which a *cis*-diaxial hydroxy-ester was largely hydrolysed whereas non-hydroxylated esters were unchanged. The four 3-acetoxy-5-alcohols of the



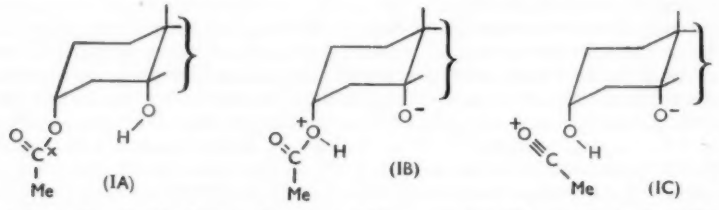
(I; 18%) (II; 70%) (III; 13%) (IV; 78%)

cholestane and coprostane series were therefore treated with potassium hydrogen carbonate solution under identical conditions—the percentage hydrolysis of each is shown below the formulæ (I)—(IV). The facilitating effect of a hydroxyl group *cis* to an ester group

• **Part I,** preceding paper.

results in the axial esters' being more rapidly hydrolysed than the equatorial esters, the usual rule [1] being reversed. 3α-Acetoxycholestane, the 5α-hydrogen analogue of ester (II), was recovered almost quantitatively after identical treatment.

These results are explicable in terms of hydrogen bonding of the 5-hydroxyl group to the alcoholic oxygen of the axial ester, a *quasi*-six-membered ring then being formed, *e.g.*,



Such an intramolecular hydrogen bond would cause a small increment of positive charge on alcoholic oxygen and on carbonyl oxygen through the extreme forms represented by (IB) and (IC). Production of forms (IB) and (IC) opposes and reduces the usual mesomeric donation of electronic charge from alcohol to carbonyl oxygen in the ester. Thus the carbonyl bond and the $C^{X}O$ bond would be expected to move to higher and to lower orders, respectively (supporting infrared evidence below), and for the former this increase in bond order is reflected in a greater reactivity towards the nucleophilic reagent employed in the hydrolyses.

The infrared absorption spectra of the acetoxy-alcohols (I)—(IV) have confirmed and amplified these suggestions. From the results (Table) it may be seen that the directions of the shifts observed with diaxial compounds conform to the presence of the postulated hydrogen bonding (C=O stretching frequency raised, C–O stretching frequency lowered). Such hydrogen bonding to the *alcoholic* oxygen of an ester is apparently unprecedented, only bonding to the *carbonyl* oxygen having been observed previously. Thus, in mixed solutions of alcohols and esters shifts of the carbonyl stretching band to lower frequencies occur, corresponding to intramolecular hydrogen bonding to carbonyl oxygen.[2] Even larger decreases in carbonyl frequency take place in salicylic esters [3] where the bonding to the carbonyl group is apparently strengthened by interactions with the aromatic ring.

The unusual occurrence of hydrogen bonding to alcoholic oxygen in esters (II) and (IV) is probably due to the formation of a *quasi*-six-membered ring in preference to a *quasi*-eight-membered ring, the atoms comprising the smaller ring being held close together in their diaxial conformation. In this connection the strength of the intramolecular bonding to alcoholic oxygen appears to be diminished in the monoesters of more flexible, *e.g.*, acyclic, 1 : 3-diols (it is hoped to amplify these observations for subsequent publication).[4] In the more complicated 17-hydroxy-20-oxo-21-acetate cortical side-chain, hydrogen bonding to alcoholic oxygen cannot be discerned.[5]

The hydroxy-esters (I)—(IV) also show regular differences in the O–H stretching region, the *trans*-compounds giving double peaks (relative intensities varying on dilution), and the *cis*-compounds giving higher-intensity single peaks. No conclusions could be drawn from an examination of the bands just above 1000 cm.$^{-1}$ where both hydroxyl and acetate absorb, except that the axial–equatorial band correlations [6] were indistinct.

[1] Barton, *Experientia*, 1950, **6**, 316.
[2] Searles, Tamres, and Barrow, *J. Amer. Chem. Soc.*, 1953, **75**, 71.
[3] Gordy, *J. Chem. Phys.*, 1940, **8**, 516; Duncanson, Grove, and Zeally, *J.*, 1953, 1331. Our own data are given in the Table, positions of the C–O bands near 1250 cm.$^{-1}$ being given apparently for the first time.
[4] With the stronger bonding occurring between two hydroxyl groups, *cyclo*hexane-*cis*-1 : 3-diol shows evidence of intramolecular bonding in the normally less favourable diaxial conformation (Kuhn, *J. Amer. Chem. Soc.*, 1952, **74**, 2492; 1954, **76**, 4323).
[5] R. N. Jones, Humphries, Herling, and Dobriner, *ibid.*, 1951, **73**, 3215.
[6] Page, *J.*, 1955, 2017, where earlier references are also given.

In more general terms the effect of hydrogen bonding on ester reactivity may be considered to have some electronic analogy with the acid anhydride–ester relation, the

Infrared absorption bands of esters (in cm.$^{-1}$)

Compound	OH stretch.	C=O stretch.	C–O stretch.	Solv.
No hydrogen bonding				
3β-Acetoxycholestane	—	1732	1236	CCl_4
3β-Acetoxycholestan-5α-ol (I)	3590, 3430	1731	1236	CCl_4
3β : 6β-Diacetoxycholestan-5α-ol	3600, 3470	1732	1240	CCl_4
3α-Acetoxycholestane	—	1733	1234 †	CCl_4
3α-Acetoxy-coprostan-5β-ol (III)	3590, 3430	1734	1237	CCl_4
Hydrogen bonding to alcohol oxygen				
3α-Acetoxycholestan-5α-ol (II)	3570	1744	1224	CCl_4
3β-Acetoxycoprostan-5-ol (IV)	3570	1745	1223	CCl_4
3β : 6β-Diacetoxycoprostan-5β-ol [b]	3580	1740 *	1230 *	CCl_4
Hydrogen bonding to carbonyl oxygen				
Methyl salicylate	3180	1677	1310, 1258, 1217	CS_2
(Cf. Methyl benzoate)	—	1721	1281	CS_2
Methyl propionate and methanol [2]	not given	1740	not given	CS_2
(Cf. Methyl propionate) [2]	—	1748	not given	CS_2

* Broad.
† Most intense band of complex peak (cf. ref. 5); the other steroid acetates gave single peaks.

Infrared absorption bands of methyl ethers (in cm.$^{-1}$)

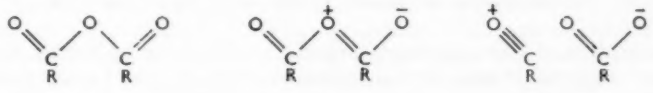
Compound	OH stretch.	C–O stretch.	Solv.
3β-Methoxycholestane [a]	—	1100	CS_2
3β-Methoxycholestan-5α-ol [b]	3580	1098	CS_2
3α-Methoxycholestane [a]	—	1086	CS_2
3α-Methoxycholestan-5α-ol [c]	3490	1080	CS_2
3α-*tert.*-Butoxycholestan-5α-ol [c]	3460	1080	CS_2

Infrared absorption of chloro-compounds (in cm.$^{-1}$)

Compound	OH stretch.	C–Cl stretch.	Solv.
3β-Chlorocholestane [d]	—	755, 710	CS_2
3β-Chlorocholestan-5α-ol [c]	3600	758, 711	CS_2
3α-Chlorocholestane [d]	—	735, 707	CS_2
3α-Chlorocholestan-5α-ol [c]	3590	732, 722, 686	CS_2

[a] Reference 6. [b] Henbest and Wilson, preceding paper. [c] Clayton, Henbest, and Smith, *J.*, 1957, 1982. [d] Barton, Page, and Shoppee, *J.*, 1956, 2017.

former being more reactive towards nucleophils due to the contribution to the ground state of forms such as (VB) and (VC) [analogous in electronic shifts to (IB) and (IC)].



(VA) (VB) (VC)

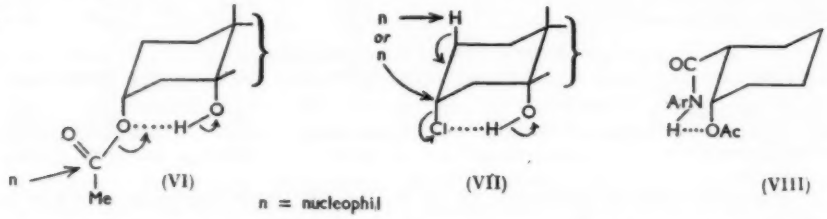
With the very reactive acyl halides the triple-bonded structure presumably provides an even larger contribution. In the infrared spectrum, these compounds also show progressive shifts of carbonyl frequency to higher values (*e.g.*, Me·CO·OMe, 1740 cm.$^{-1}$; Me·CO·O·COMe, 1824 and 1748 cm.$^{-1}$; Me·COCl, 1802 cm.$^{-1}$).

Marked hydrogen bonding occurs also with other 3α-substituted-5α-hydroxy-steroids. Thus 3α-methoxycholestan-5α-ol gives in the hydroxyl stretching region a more intense peak at somewhat lower frequency than that given by 3β-methoxycholestan-5α-ol; the peak near 1100 cm.$^{-1}$ is also shifted slightly. The 3α-methoxy-5α-alcohol is also eluted

from alumina very much more easily than its *trans*-isomer, similar ease of elution being observed with the *cis*-acetate-alcohols (II) and (IV).

Alkyl halides are not usually considered to form hydrogen bonds very effectively with alcohols, but the juxtaposition of chlorine and hydroxyl in 3α-chlorocholestan-5α-ol causes appreciable bonding: the *cis*-compound again gave a more intense hydroxyl peak at a lower frequency than the *trans* isomer. Introduction of a 5α-hydroxyl group into 3α-chlorocholestane causes marked alterations in the positions and intensities of the carbon–chlorine stretching bands in the 750—650 cm.$^{-1}$ region: no appreciable changes were observed in the 3β-chloro-5α-series.

Facilitation of ester hydrolysis by a neighbouring hydroxyl group is explicable in terms similar to the termolecular (push-pull) concept of many S_N reactions in solution, *i.e.*, the 5-hydroxyl group provides the necessary electrophilic component for the displacement



at the carbonyl carbon atom, its adjacent position and partial bonding to the alcoholic oxygen atom assisting the development of the transition state as the nucleophil approaches (VI). With the 3α-chloro-5α-alcohol, reactions involving displacement of chlorine (as chloride) from $C_{(3)}$ should be similarly assisted (cf. VII). Preliminary observations have shown that hydrogen chloride is eliminated by pyridine much more rapidly from the *cis*-chloro-alcohol than from the corresponding 5-hydrogen compound. The reaction of the chloro-alcohol with pyrrolidine is also faster.

By contrast to intramolecular nucleophilic facilitation processes, assistance of S_N reactions by neighbouring electrophils has received little attention. A more complex example is the elimination of glycollic acid from strychninolic acid, which depends [7] on the appropriate configuration of a nearby hydroxyl group. Hydrogen bonding has been suggested [8] to account for the greater reactivity of *cis*- than of *trans*-2-hydroxy*cyclo*hexanecarboxylic acid derivatives. The more rapid hydrolysis of the *cis*-acetoxy-*p*-toluidide (VIII) being taken as example, it can be surmised that hydrogen bonding is more effective with the *cis*-compound, a quasi-*cis*-bicyclic structure being formed more easily. The preference for ring formation in such *cis*-structures where oxygen substituents (axial to the *cyclo*hexane ring) are involved is of course supported by a number of observations concerned with the formation of stable cyclic derivatives (lactones, *iso*propylidene derivatives, etc.).

Since publication of our preliminary report [9] on the ester hydrolysis Kupchan and Johnson have suggested [10] that the configuration of the $C_{(16)}$ hydroxyl group in cevine should be reversed (axial instead of equatorial), the ready hydrolysis of the $C_{(16)}$-esters being assisted by the nearby axial $C_{(20)}$ hydroxyl group.

[*Added, March 4th*, 1957.—The fact that the acid-catalysed dehydration of a steroid 8α-hydroxyl group takes place more readily when a 5α-hydroxyl group is also present than with the 5α-hydrogen analogue appears to provide another example of the phenomenon (Hallsworth and Henbest, unpublished work). Dr. R. C. Cookson has

[7] Woodward quoted by Holmes in "The Alkaloids," Academic Press Inc., New York, 1952, Vol. II, p. 517.
[8] Pascual, Sistaré, and Regás, *J.*, 1949, 1943.
[9] Henbest and Lovell, *Chem. and Ind.*, 1956, 278.
[10] Kupchan and Johnson, *J. Amer. Chem. Soc.*, 1956, **78**, 3864.

drawn our attention to the observations of Bartlett and Greene (*J. Amer. Chem. Soc.*, 1954, **76**, 1088), who found that the rate of alkaline hydrolysis of methyl triptoate is accelerated markedly on introduction of a 2α-hydroxyl group.]

Experimental

Hydrolysis of the Acetoxy-alcohols (I—IV).—The steroid (60 mg.) in benzene (1 c.c.) and methanol (4 c.c.) was treated with a solution of potassium hydrogen carbonate (7 mg.) in water (0·5 c.c.), the clear solution being kept at 20° for 65 hr. The product from each reaction was chromatographed on deactivated alumina: the m. p. of each crude product and the yield of each diol obtained on chromatography are tabulated.

Acetoxy-alcohol	M. p.	Crude product, m. p.	Pure diol, m. p.	Diol yield
(I)	184—186°	182—186°	220—223°	18%
(II)	136—138	191—198	197—220	70
(III)	145—148	139—148	184—189	13
(IV)	79—81	78—125	144—146	78

In a similar experiment, 3α-acetoxycholestane (100 mg.) (m. p. 97—98°) in benzene (3 c.c.) and methanol (15 c.c.) was treated with potassium hydrogen carbonate (25 mg.) in water (2 c.c.). Isolation of the product after 65 hr. gave unchanged material (98 mg.), m. p. 95—99°.

This work was carried out during the tenure of a grant (to B. J. L.) from Glaxo Laboratories Ltd.

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[*Received, November 7th*, 1956.]

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378. *Aspects of Stereochemistry. Part III.* Metal Reduction of Some Allylic Systems.*

By A. S. Hallsworth, H. B. Henbest, and T. I. Wrigley.

Lithium–ethylamine reduction of an optically active carvotanacetyl methyl ether yields racemic *p*-menth-1-ene showing that the reaction proceeds *via* a symmetrical intermediate. Conversion of an allylic alcohol into an olefin is often conveniently performed by metal–amine reduction of an ester, although if the hydroxyl group is hindered prior formation of an ester or ether may not be necessary.

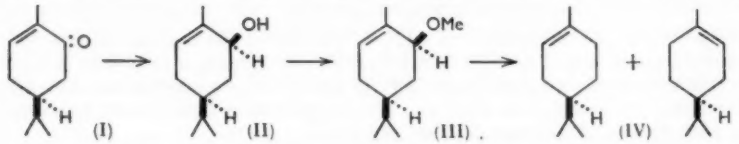
Seeking improved routes to certain olefins in the steroid series, we focused our interest on reduction of allylic systems by dissolving metals. Previous work,[1,2] mainly with sodium–ammonia, has demonstrated that allylic alcohols afford olefins or olefin mixtures, often accompanied by the dihydro-alcohol. Allylic ethers also yield olefins but no observations have been reported on the more easily prepared allylic esters.[3]

After migration of the olefinic bond during reduction had been observed in the steroid series, the nature of the intermediate stage was examined by reduction of a simpler system, (+)-*cis*-carvotanacetol (II) [readily prepared from (+)-carvone], where the extent of rearrangement on reduction could be ascertained from the optical rotation of the *p*-menth-1-ene produced, as the original and the rearranged olefin are enantiomorphic (IV). Reduction of the methyl ether (III) of (+)-*cis*-carvotanacetol gave racemic *p*-menthene (IV), the reaction proceeding therefore *via* a symmetrical intermediate. This intermediate is probably best regarded as a mesomeric carbanion resulting from successive addition of two electrons to the ether (III) (cf. Birch [1]).

* Part II, preceding paper.

[1] Birch, *Quart. Rev.*, 1950, **4**, 69.
[2] Watt, *Chem. Rev.*, 1950, **46**, 330.
[3] Part of this work was described in a preliminary note, *Chem. and Ind.*, 1956, 522.

The (+)-*cis*-carvotanacetol (II) was prepared by reduction with lithium aluminium hydride of (+)-carvotanacetone (I), the *cis*-alcohol (predominant in the mixture) being separated as its *p*-nitrobenzoate. Previous workers [4] had reduced (+)-carvotanacetone by the Ponndorf method obtaining the high-melting *p*-nitrobenzoate as the main product



and the *cis*-isomer only as by-product. From optical-rotation data Mills [5] has suggested that the higher-melting ester is a *cis–trans*-mixture, and the lower melting the pure *cis*-ester. For the lithium reduction it was desirable to use a single geometrical isomer, and the obtaining by reduction with hydride of an apparently much higher proportion of the *cis*-alcohol (II) was therefore advantageous. As allylic esters, *e.g.* benzoates, are usually reduced by lithium to olefins (below), reduction of the intermediate *cis*-*p*-nitrobenzoate was also attempted. No hydrocarbon was isolated and a red colour developed in place of the usual blue, indicating preferential attack on the nitro-group. Reduction with lithium of the *cis*-alcohol itself was not attempted as previous work [1] and our own results with steroids (below) had established that the reduction is more difficult and that prolongation of the reaction time was not desirable as isolated olefinic bonds can be reduced by dissolving metals.[6–8]

In the steroid series the reaction was studied in search for an improved route to cholest-4-ene (VI). Reduction by lithium aluminium hydride of cholest-4-en-3-one gave an alcohol mixture from which the major component, the 3β-alcohol, could be readily obtained as the benzoate (V; R = Bz). A good yield of cholest-4-ene was then obtained by reduction of the benzoate with lithium, and high yields were also obtained by similar reduction of the acetate and methyl ether (V; R = Ac and Me, respectively). Cholest-4-ene so obtained does not require purification *via* the dibromide, and this together with the reproducibility of the method represent improvements over the previous mercaptal route. In these reductions alternative reactions of the Bouveault–Blanc type (regenerating the 3β-alcohol) do not occur significantly. The assistance given by the double bond was shown by reduction of cholestanyl benzoate, cholestanol but no cholestane being produced.

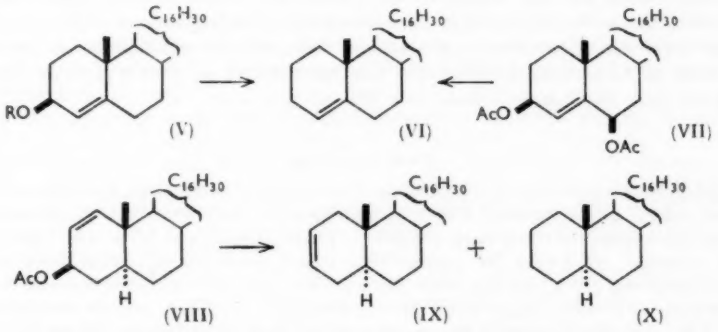
Reduction of the diacetoxy-olefin (VII) yielded slightly less pure cholest-4-ene. With this diester some cholest-5-ene might be formed by initial reductive scission of the 3-ester group followed by further reaction *via* the $C_{(4)}$–$C_{(5)}$–$C_{(6)}$ allylic carbanion.

The general procedure for these experiments was to add an excess of lithium to a solution of the compound in ethylamine.[8] Most steroids are moderately soluble in this amine but only sparingly soluble in boiling liquid ammonia.[9] Thus addition of an ethereal solution of the 3β-benzoate (V; R = PhCO) to lithium dissolved in ammonia gave only a low yield of cholest-4-ene, most of the ester being unchanged owing to precipitation. Reduction by lithium–ethylamine of the 3β-alcohol (V; R = H) afforded mostly starting material together with about 10% of cholest-4-ene : in this case the alcohol is probably converted rapidly into the difficultly reducible anion.

Cholest-2-ene (IX) is more stable than cholest-1-ene ; [10,11] in the preparation of the latter from 3β-chlorocholest-1-ene, rearrangement could be avoided only by reduction with

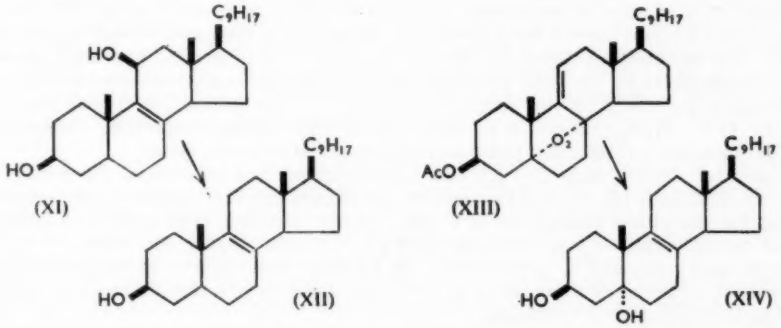
[4] Read and Swann, *J.*, 1937, 239.
[5] Mills, *J.*, 1952, 4976.
[6] King, *J.*, 1951, 898.
[7] Greenfield, Friedel, and Orchin, *J. Amer. Chem. Soc.*, 1954, **76**, 1258.
[8] Benkeser, Sauve, and Schroll, *ibid.*, 1955, **77**, 3378.
[9] Birch, *J. Proc. Roy. Soc. N.S.W.*, 1949, **83**, 249.
[10] Henbest, Meakins, and Wood, *J.*, 1954, 800.
[11] Turner, XIVth Internat. Congr. Pure and Applied Chem., 1955, Abs. paper 594.

lithium aluminium hydride in a poorly ionising solvent.[12] As reduction with metal–amine proceeds *via* mesomeric carbanions it was not surprising to obtain cholest-2-ene from reduction by lithium of 3β-acetoxycholest-1-ene (VIII). The course of this part of the reaction is thus controlled thermodynamically and not by ease of access of the proton donor to the intermediate carbanion [$C_{(1)}$ more hindered than $C_{(3)}$]. Cholestane (X) was the other product identified: its origin is uncertain as both cholest-1- and -2-enes are reduced to the saturated hydrocarbon by treatment with a large excess of lithium in ethylamine.



The only previous method of obtaining Δ^8-steroids (apart from some rather inaccessible natural steroids, *e.g.* zymosterol) involved hydrogenation of an 8 : 14-diene to a mixture of Δ^8- and $\Delta^{(8)14}$-olefins followed by a fractional crystallisation.[13]

For the new method, a Δ^8-11-ketone (of the ergostane series) was first reduced by lithium aluminium hydride to the 3β : 11β-diol (XI). This with lithium–ethylamine then afforded the Δ^8-compound (XII). Careful hydrogenation of its acetate then reduced the side-chain double bond to give the known 3β-acetoxyergost-8-ene. The more complete reduction of this 11-hydroxy-group, compared with that of the 3β-alcohol (V; R = H) described previously, may be a consequence of its more hindered position ensuring by steric inhibition of anion solvation [14] that not all of the 11-alcohol is in the (more heavily solvated) unreactive anionic form. Reduction of the 3β : 11β-diol was attempted as difficulty was expected in the preparation of esters or ethers from the hindered alcohol because of the ease of dehydration to the 7 : 9-diene.



Reduction by lithium of an 8-oxygenated-$\Delta^{9(11)}$-system should proceed *via* a similar $C_{(8)}$–$C_{(9)}$–$C_{(11)}$ anion and in agreement with this, the epidioxide (XIII) also afforded a

[12] Henbest and Wilson, *J.*, 1956, 3289.
[13] Barton and Cox, *J.*, 1949, 214.
[14] Cf. H. C. Brown, *J.*, 1956, 1248.

Δ^8-compound (XIV) (fission of the O–O bond probably first occurring). In this case the Δ^8-structure is assigned on the basis of ultraviolet absorption [15] and molecular-rotation data.[13] In contrast to the corresponding 5-hydrogen compound, the double bond was not isomerised into the $\Delta^{8(14)}$-position on prolonged shaking with hydrogen–platinum–acetic acid; the double bond in a Δ^7-5α-alcohol migrates to the $\Delta^{8(14)}$-position under these conditions,[16] but noticeably more slowly than in the 5-hydrogen compound.

An advantage of these methods over the previous route to Δ^8-compounds is that side-chain double bonds are not reduced; the procedure should thus be adaptable to the synthesis of natural Δ^8-compounds of the steroid and trimethylsteroid series.

[*Added later on Manuscript.*—Reduction with lithium–ethylamine of 4β-acetoxycholest-5-ene or 6β-acetoxycholest-4-ene has been found to give a similar mixture of cholest-4-ene (45—50%) and cholest-5-ene (50—55%).]

Experimental

(+)-cis-*Carvotanacetol* (II).—(+)-Carvone (from caraway oil) was hydrogenated in the presence of Adams's catalyst until 1 mol. of hydrogen had been absorbed. Purification of the product *via* its bisulphite compound yielded (+)-carvotanacetone, b. p. 105—106°/17 mm., $[\alpha]_D$ +56° (homog.), n_D^{20} 1·4794 {lit. values [4] $[\alpha]_D$ +55·2° (homog.), n_D^{21} 1·4791}. A solution of (+)-carvotanacetone (10 g.) in dry ether (20 c.c.) was added to a stirred solution of lithium aluminium hydride (0·85 g.) in dry ether (30 c.c.) during 0·5 hr. The mixture was heated under reflux for 1 hr., and then treated with an excess of 5% sodium hydroxide solution. The ether solution yielded the carvotanacetol mixture (9·8 g.), which (9 g.) in light petroleum (150 c.c.) containing pyridine (5·1 g.) was treated (with stirring) with a solution of *p*-nitrobenzoyl chloride (11 g.) in dry benzene (75 c.c.), the temperature being kept below 35°. After being stirred for 3 hr. the solution was shaken with water (100 c.c.) and filtered. After being washed with 5% sodium hydroxide solution and dried, the solution was evaporated to give the ester mixture (14·5 g.). This was separated by fractional crystallisation from light petroleum into the *cis*-ester (5·5 g.) (more soluble), m. p. 60—61°, $[\alpha]_D$ −51° (in $CHCl_3$), $[\alpha]_D$ −32° (in benzene), and the higher-melting ester (probably *cis–trans* mixture), m. p. 93—94°. For the lower-melting ester Read and Swann [4] record m. p. 60—62°, $[\alpha]_D$ −51° (in $CHCl_3$).

A solution of the *cis*-ester (5 g.) in methanolic potassium hydroxide solution (42 c.c.; 5%) was heated under reflux for 10 min. Most of the methanol was removed under reduced pressure and the carvotanacetol isolated with light petroleum. Distillation gave pure (+)-cis-*carvotanacetol* (2·3 g.), b. p. 64°/0·5 mm., m. p. 22°, $[\alpha]_D$ +56·5° (in benzene) (Found: C, 77·8; H, 11·7. $C_{10}H_{18}O$ requires C, 77·9; H, 11·8%).

Preparation and Reduction of (+)-cis-*Carvotanacetyl Methyl Ether* (III).—The alcohol (2 g.) was added to a solution of potassium *tert.*-butoxide [from potassium (5·1 g.) and *tert.*-butyl alcohol (130 c.c.)] and methyl iodide (18·5 g.; 10 mol.) was then added with stirring during 15 min. The mixture was stirred for 2 hr. and the product then isolated with light petroleum. It was remethylated by the same procedure and the product finally fractionated to give pure *methyl ether* (0·9 g.), b. p. 63—64° (bath)/1 mm., $[\alpha]_D$ +70° (in benzene), n_D^{20} 1·4653 (Found: C, 78·3; H, 11·8. $C_{11}H_{20}O$ requires C, 78·5; H, 12·0%). Infrared spectrum confirmed the presence of methoxyl (1100 $cm.^{-1}$ band) and the absence of hydroxyl group.

Freshly cut lithium slices (0·4 g.) were added rapidly to a solution of the methyl ether (0·8 g.) in ethylamine (25 g.), and the mixture was shaken mechanically for 5 min. longer than required for the initial appearance of a blue colour. Isolation with ether and distillation afforded optically inactive *p*-menth-1-ene (0·36 g.), b. p. 175° (bath), n_D^{21} 1·4570 (lit. values [17] for the racemic compound b. p. 174—175°, n_D^{21} 1·4551). The infrared spectrum of the olefin was identical with that of a sample of (+)-*p*-menth-1-ene, $[\alpha]_D$ +105° (homog.). prepared by partial hydrogenation of (+)-limonene.

Concentrated hydrochloric acid (0·35 c.c.) was added to a mixture of the hydrocarbon (0·3 g.; from the reduction), pentyl nitrite (0·3 g.), and acetic acid (0·1 c.c.) so that the temperature did not rise above −10°. After the mixture had been kept at −15° for 10 min., the

[15] Bladon, Henbest, and Wood, *J.*, 1952, 2737.
[16] Clayton, Henbest, and Jones, *J.*, 1953, 2015.
[17] Wallach, *Annalen*, 1911, **381**, 58.

XUM

solid product (0·225 g.) was collected. Crystallisation from acetone gave the pure optically inactive nitrosochloride, m. p. 94—95° (lit. value [17] m. p. 95—96°, for the racemic compound).

General Technique for Reduction of Steroids by Lithium–Ethylamine.—The steroid was dissolved in dry ethylamine in a glass-stoppered bottle. Small pieces of freshly cut lithium were added and, when the initial effervescence had ceased, the stopper was fitted firmly and the mixture shaken vigorously until a blue colour persisted. The bottle was cooled to 0° before opening, the steroid then being isolated with ether in the usual way. As considerable pressure develops, a tube with stopcock was often used in place of the stopper for periodical release of pressure.

Cholest-4-ene (VI).—(*a*) 3β-Acetoxycholest-4-ene (0·4 g.) was reduced with lithium (0·1 g.) in ethylamine (20 c.c.). The product was isolated and a light-petroleum solution filtered through alumina (25 g.) to give material which on crystallisation from methanol–acetone gave cholest-4-ene (0·325 g.), m. p. 83—84°, $[\alpha]_D$ +73°.

(*b*) Similar reduction of 3β-methoxycholest-4-ene (0·195 g.) with lithium (0·1 g.) in ethylamine (15 c.c.) afforded cholest-4-ene (0·147 g.), m. p. 82—83°, $[\alpha]_D$ +73°.

(*c*) Reduction of 3β-benzoyloxycholest-4-ene (0·4 g.; see below) with lithium (0·1 g.) in ethylamine yielded cholest-4-ene (0·224 g.), m. p. 83—84°, $[\alpha]_D$ +75°. Material prepared by the thiol method followed by purification *via* the dibromide [18] had m. p. 82—83·5°, $[\alpha]_D$ +76°.

(*d*) Reduction of 3β : 6β-diacetoxycholest-4-ene (0·4 g.) with lithium (0·2 g.) in ethylamine (20 c.c.) gave cholest-4-ene (0·286 g.), m. p. 77—79°, $[\alpha]_D$ +68°.

(*e*) Cholest-4-en-3β-ol (0·26 g.) was reduced with lithium (0·1 g.) in ethylamine (15 c.c.), and the product (0·236 g.) was chromatographed on deactivated alumina (20 g.). Elution with light petroleum gave cholest-4-ene (35 mg.), m. p. 81—82°. Elution with benzene–ether (4 : 1) afforded starting alcohol (0·147 g.), m. p. and mixed m. p. 132—134°.

Reduction of Cholestanyl Benzoate.—The steroid (0·2 g.) was reduced with lithium (50 mg.) in ethylamine (10 c.c.) by the general technique. Chromatography of the product on alumina (10 g.) did not give a hydrocarbon fraction, but elution with benzene–ether (9 : 1) afforded cholestanol (0·11 g.), m. p. and mixed m. p. 140—141°.

3β-*Benzoyloxycholest-4-ene* (V; R ≡ Bz).—A solution of cholest-4-en-3-one (30 g.) and lithium aluminium hydride (5 g.) in dry ether (500 c.c.) was heated under reflux for 30 min. The steroid was isolated with ether and then treated with an excess of benzoyl chloride in pyridine at 20° for 15 min. Two crystallisations from methanol–acetone gave the pure *benzoate* (22 g.), m. p. 125—128°, $[\alpha]_D$ 0° (Found : C, 83·5; H, 10·3. $C_{34}H_{50}O_2$ requires C, 83·2; H, 10·3%).

Reduction of 3β-*Acetoxycholest-1-ene* (VIII).—The steroid (0·232 g.) was reduced with lithium (0·15 g.) in ethylamine (15 c.c.) (solution blue for 5 min.). The infrared spectrum of the product showed the presence of cholest-2-ene (peaks at 664 and 773 cm.$^{-1}$) and the virtual absence of cholest-1-ene (no peaks at 700 and 718 cm.$^{-1}$). A solution of the product (0·147 g.) and osmium tetroxide (0·15 g.) in ether (20 c.c.) and pyridine (5 c.c.) was kept at 20° for 3 days, then evaporated to dryness under reduced pressure, and the residue treated with an excess of lithium aluminium hydride in boiling ether solution. This material (0·107 g.) was chromatographed on deactivated alumina (10 g.). Light petroleum eluted cholestane (37 mg.), m. p. and mixed m. p. 79—81°; the infrared spectrum was identical with that of an authentic sample. Elution with ether–methanol (5 : 1) afforded cholestane-2α : 3α-diol [19] (47 mg.), m. p. and mixed m. p. 209—213°.

Cholest-1-ene (17 mg.) in ethylamine was treated with lithium (50 mg.) for 35 min. (blue for 15 min.). The infrared spectrum of the product showed the presence of only a small percentage of starting material. After treatment of the total product with osmium tetroxide as described above, pure cholestane (9 mg.), m. p. and mixed m. p. 79—81°, was obtained. In a similar experiment with cholest-2-ene (31 mg.), cholestane (24 mg.) was obtained.

Reduction of Ergosta-8 : 22-diene-3β : 11β-diol (XI).—The diol was prepared by heating a solution of 3β-acetoxy-11-oxoergosta-8 : 22-diene (0·77 g.) and lithium aluminium hydride (0·3 g.) in ether (100 c.c.) under reflux for 1 hr. Excess of reagent was decomposed with water, and the precipitated hydroxides were washed repeatedly with ether. Evaporation of the dried ether solution gave material (0·68 g.) which on crystallisation from acetone afforded the pure *diol*, m. p. 161—163°, $[\alpha]_D$ +2° (Found : C, 80·95; H, 11·25. $C_{28}H_{46}O_2$ requires C, 81·1; H,

[18] Bladon, Fabian, Henbest, Koch, and Wood, *J.*, 1951, 2402.
[19] Henbest and Smith, *J.*, 1957, 926.

XUM

11·2%). This compound showed no light absorption in the 2400—2500 Å region. Mild acetylation gave the 3β-*monoacetate* (plates from acetone), m. p. 173—184°, $[\alpha]_D$ +12° (Found: C, 79·0; H, 10·7. $C_{30}H_{48}O_3$ requires C, 78·9; H, 10·6%). Heating a solution of this compound in acetic acid–acetic anhydride at 100° for 1 hr. gave 3β-acetoxyergosta-7 : 9 : 22-triene.

For reduction, the 3 : 11-diol (1·31 g.) in ethylamine (25 c.c.) was treated with lithium (0·4 g.), the mixture being shaken until the blue colour disappeared. The product (1·05 g.) was twice crystallised from acetone to give *ergosta*-8 : 22-*dien*-3β-*ol* (XII) (0·76 g.), m. p. 166—169°, $[\alpha]_D$ +30° (Found: C, 84·0; H, 11·45. $C_{28}H_{46}O$ requires C, 84·35; H, 11·65%). The *acetate* had m. p. 167—169°, $[\alpha]_D$ +14° (Found: C, 81·85; H, 10·7. $C_{30}H_{48}O_2$ requires C, 81·75; H, 11·0%). This acetate (0·59 g.) in ethyl acetate (50 c.c.) was shaken with hydrogen and Adams's catalyst for 2 hr. Isolation of the pure product yielded 3β-acetoxyergost-8-ene (0·39 g.), m. p. 156—158°, $[\alpha]_D$ +22° (lit. values [13] m. p. 156—157°, $[\alpha]_D$ +22°).

Ergost-8-*ene*-3β : 5α-*diol* (XIV).—3β-Acetoxy-5α : 8α-epidioxyergost-9-ene (XIII) (2 g.) dissolved in ethylamine (100 c.c.) was reduced by the general technique except that further quantities of lithium were added in order to preserve a blue colour during 4 hours' shaking. The product (1·7 g.) on crystallisation from ethyl acetate–methanol yielded the *diol*, m. p. 215—226°, $[\alpha]_D$ +34° (Found: C, 80·75; H, 11·5. $C_{28}H_{48}O_2$ requires C, 80·7; H, 11·6%). Experiments had shown that longer reduction was necessary in this case, samples of the crude product being heated in ethanol containing a little hydrochloric acid to determine unchanged 8α-hydroxy-Δ^9-compound as 7 : 9-diene, the reduction being assumed to proceed *via* the 5α : 8α-diol.

Acetylation of the diol at 20° afforded 3β-*acetoxyergost*-8-*en*-5α-*ol* (needles from methanol), m. p. 188—190°, $[\alpha]_D$ +20° (Found: C, 78·7; H, 11·1. $C_{30}H_{50}O_3$ requires C, 78·55; H, 11·0%). Ultraviolet end absorption (in EtOH): $\varepsilon_{2100} = 4400$; $\varepsilon_{2150} = 3900$; $\varepsilon_{2200} = 3400$. Normal benzoylation gave 3β-*benzoyloxyergost*-8-*en*-5α-*ol*, m. p. 165—167°, $[\alpha]_D$ +30° (Found: C, 80·5; H, 10·2. $C_{35}H_{52}O_3$ requires C, 80·7; H, 10·1%).

The $[M]_D$ changes on acetylation and benzoylation are −50° and +14°, respectively, in good agreement with those given [13] for the 5α-hydrogen series, −46° and +15°, respectively.

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379. *Aspects of Stereochemistry. Part IV.* The Steric Requirement for Hydrogen–Catalyst Induced Migration of the Olefinic Bond.*

By J. B. Bream, D. C. Eaton, and H. B. Henbest.

For the isomerisation of an olefinic bond under hydrogenation conditions a *cis*-relation should exist between the entering and leaving hydrogen atoms, and both must be sterically accessible to the catalyst surface. The phenomenon is discussed with particular reference to some new experiments with 8α- and 14β-steroids. Comment is also made upon the greater stability of 1-alkyl*cyclo*pentenes compared with their exocyclic isomers.

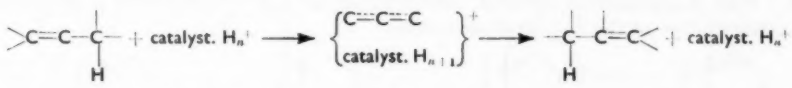
Most olefins can be hydrogenated in the presence of a catalyst to saturated compounds. However, if the olefinic bond is tri- or tetra-alkylated and in a very hindered position (*e.g.* $\Delta^{8(14)}$-steroids, α- and β-amyrins) addition may be impossible under the normal experimental conditions. This paper is concerned with the region between these two extremes, where, for a given olefinic position, either addition or isomerisation to a more stable olefin takes place, the choice of reaction depending on the stereochemical environment of the olefin.

Perhaps the best-known examples [1] of the isomerisation reaction are the conversion of

* Part III, preceding paper.

[1] Fieser and Fieser, "Natural Products Related to Phenanthrene," Reinhold Publ. Corp., New York, 1949, p. 240. Partial steroid formulæ are used throughout this paper in order to emphasize rings B and C.

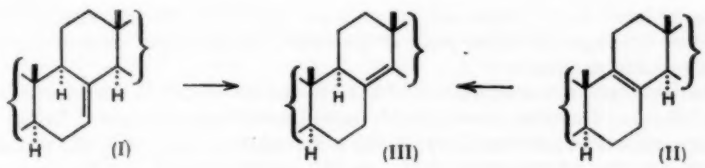
Δ^7- and Δ^8-steroids (I and II, respectively) into $\Delta^{8(14)}$-compounds (III) in the presence of hydrogen and palladium or less effectively platinum. These reactions are more rapid in the presence of weak acids (*e.g.*, acetic acid, not sufficiently strong to cause isomerisation by ordinary solution prototropy), and this fact, together with stereochemical evidence discussed below, leads to the suggestion that a simple picture of the reaction may involve the formation of an allylic carbonium ion–catalyst complex as intermediate stage. An

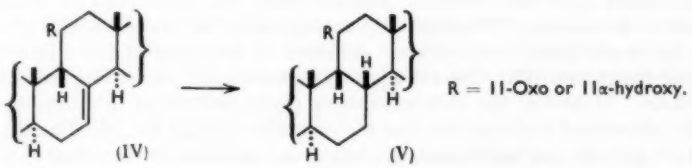


alternative rôle of acid could be initial addition of a proton to give an intermediate "saturated" carbonium ion; the greater general stability of allylic carbonium ions would appear to make them preferable as intermediates.

Isomerisation of a double bond in the presence of hydrogen and catalyst usually takes place with tri- and tetra-substituted olefins.[2] From the examples discussed in this paper it is concluded that for isomerisation to occur (*a*) the allylic hydrogen to be removed must be sterically accessible to the catalyst surface and (*b*) there must be a favourable energy change for the re-entry of hydrogen on the *same* side of the molecule to give an olefin which does not add hydrogen. Thus, with factor (*a*) a reversal of configuration of allylic hydrogen may cause it to become relatively inaccessible to the catalyst, and normal addition of hydrogen may then take place.

In the isomerisation of a Δ^7- or Δ^8-5α-steroid (I or II), the catalyst operates on the rear (α) side of the molecule, well known to be less hindered in compounds with the given stereochemistry. The *cis*-removal and addition of hydrogen on the α-face is easily seen in the conversion of (II) into (III), but complete proof in the conversion of (I) into (III)





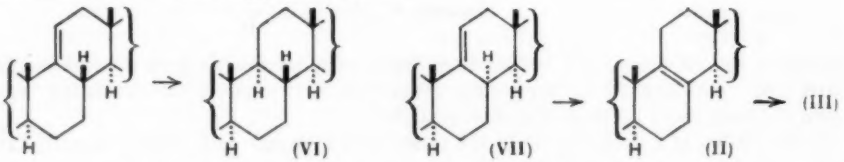
requires the configurational identification of the hydrogen atom added at $C_{(7)}$. It should be possible to test this by using deuterium in place of hydrogen and determining the configuration of the $C_{(7)}$-deuterium (it should be axial 7α) by infrared spectral methods.[3] If the catalyst were not prevented by steric factors from approaching the top (β) face of the Δ^7-compound (I), normal addition at this face would give an all-*trans*–*anti*-molecule with

[2] Howe and McQuillin (*J.*, 1956, 2670) showed that prior isomerisation of 1 : 1-disubstituted olefins to tetrasubstituted olefins takes place in the addition of hydrogen to some 6-*epi*cyperone compounds. Replacement of allylic hydrogen by deuterium occurs in the deuteration of Δ^8-steroids (Fukuchima and Gallagher, *J. Amer. Chem. Soc.*, 1955, **77**, 139). The observations are also explicable in terms of the initial formation of allylic carbonium ion-catalyst complexes.

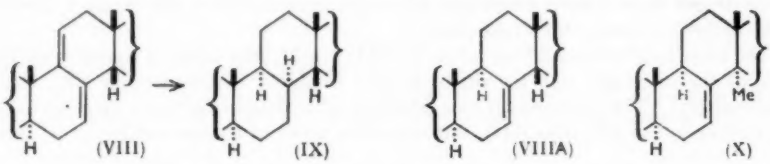
[3] Corey, Howell, Boston, Young, and Sneen, *J. Amer. Chem. Soc.*, 1956, **78**, 5036.

thermochemical stability as great as (probably greater than) that of the $\Delta^{8(14)}$-compound (III) actually formed.

Inversion of the $C_{(9)}$-configuration in the Δ^7-steroid (I) gives a 9β-steroid (IV) in which the steric factors are profoundly altered, for addition of hydrogen [4] now occurs readily at the β-face to yield the saturated system (V). The accessibility of the top face seems to be caused by bending of the molecule, the bulky angular methyl groups being moved farther apart. With β-approach of catalyst, isomerisation to a $\Delta^{8(14)}$-compound is precluded by the α-configuration of the $C_{(14)}$-hydrogen atom.



The rear face of Δ^9-5α-steroids is known to be the less hindered, and hydrogenation proceeds readily to give 9α-compounds (VI). In contrast, attempted hydrogenation of the 8α-isomer (VII; preparation below) has now been found to give a $\Delta^{8(14)}$-olefin (III), obviously *via* the Δ^8-compound (II). Models indicate that the angular methyl groups

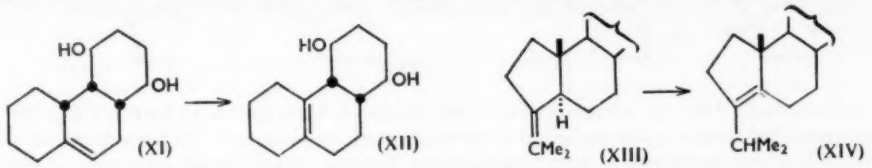


shield the Δ^9-bond from β-approach of reagents, and thus the rearrangement of (VII) to (II) can be envisaged as taking place at the α-face, the hydrogen atom at $C_{(8)}$ having the appropriate α-configuration.

Another example is hydrogenation of the 14β-steroid (VIII) to a saturated compound (IX; see below). There are three possible mono-olefinic intermediates. Initial formation of a Δ^9-compound does not seem likely as the α-approach of catalyst would probably cause isomerisation to the Δ^8-steroid (cf. VII ⟶ II), and this would not be expected to add hydrogen in view of its tetrasubstituted position in the centre of the molecule—although *cis*-addition would give the observed product (IX), the 14β-hydrogen ensuring non-isomerisation to the stable $\Delta^{8(14)}$-olefin. By analogy with the 14α-series, the Δ^7-compound (VIIIA) is the most likely intermediate. Addition of hydrogen at the α-face then gives the saturated compound (IX), the 14β-hydrogen atom again preventing isomerisation to the $\Delta^{8(14)}$-olefin. However, the stereochemistry (8α-hydrogen) of this intermediate and the fact that attempted hydrogenation of the somewhat similar 9α : 14α-dimethyl-Δ^7-compound (butyrospermol; partial formula X) results in migration on the α-face of the double-bond to the Δ^8-position,[5,6] show that isomerisation of the probable intermediate (VIIIA) to the corresponding Δ^8-steroid (which may or may not add hydrogen) should not be precluded. No final decision can be made at present on whether addition of hydrogen takes place directly to the Δ^7-bond or after its isomerisation to the Δ^8-position, although the former route may be favoured on steric grounds. A tentative explanation of the difference between the Δ^7-compound (VIIIA) which probably adds hydrogen and butyrospermol in which the bond migrates may be provided by the postulate that the addition reaction requires a more intimate olefin–catalyst association than the isomerisation

[4] Bladon, Henbest, Jones, Lovell, Wood, and Woods; Elks, Evans, Hathway, Oughton, and Thomas, *J.*, 1953, 2931.
[5] Dawson, Halsall, Jones, Meakins, and Phillips, *J.*, 1956, 3172.
[6] Lawrie, Hamilton, Spring, and Watson, *J.*, 1956, 3272.

reaction—in the present case the 14α-methyl group in butyrospermol inhibits addition. This suggestion appears reasonable when it is considered that the phenomenon of isomerisation instead of addition is encountered only in somewhat sterically hindered olefins.



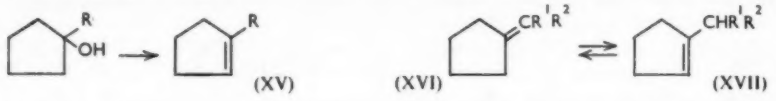
A further example of the isomerisation in which the compounds involved are of established stereochemistry, is the conversion by hydrogen–palladium of the unsaturated diol (XI) into the isomer (XII), observed in the hydrophenanthrene series.[9] The initial molecule (XI) is partly folded in a way favouring approach by catalyst on the same side as the angular hydrogen atoms; the stereochemical requirement for isomerisation is therefore present. Conversion [10] of the *iso*propylidene compound (XIII; anhydro-oleanolic lactone series) into its *cyclo*pentenyl isomer (XIV) in presence of hydrogen and palladium provides another example of the reaction: hydrogen removal takes place from the less-hindered side of the molecule, re-entry of hydrogen not creating a centre of asymmetry in this case.

Included in a generalisation recently made by Brown, Brewster, and Schechter [11] was the statement that "reactions will proceed in such a manner as to favour the formation or retention of an exo double bond in a 5-ring." The isomerisation (XIII) ⟶ (XIV) provides but one example of the many exceptions to this rule; in fact for most five-membered ring systems the rule is more accurately stated as its converse. This is not surprising as there is less eclipsing of the side-chain with ring methylene groups in the endocyclic than in the exocyclic isomer.

Thus only 1-alkyl*cyclo*pentenes (XV) have been identified in the products of dehydration of 1-alkyl*cyclo*pentanols,[12–19] and moreover in the *iso*propyl–*iso*propylidene compounds Wallach and Fleischer [20] isomerised the exocyclic to the endocyclic isomer with dilute acid. None of these simple observations was referred to by Brown, Brewster, and Shechter who mentioned the paucity of examples to support their generalisation for *cyclo*pentane systems. The work of Kon and Linstead and their collaborators referred to by these authors really indicated that in the equilibrium (XVI) ⇌ (XVII) the former was more stable only when very effective conjugation was achieved with R^1 = acetyl or carboxylic ester (R^2 = methyl or hydrogen), for with R^1 = carboxylic acid (? or derived anion) the endocyclic structure (XVII) was favoured at equilibrium. Exocyclic olefins have only been prepared by methods [20–24] (*e.g.*, pyrolysis of suitable βγ-unsaturated acids) precluding

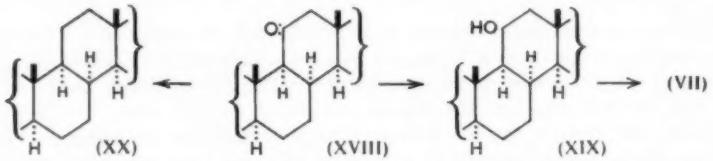
[7] Barton and Cox, *J.*, 1949, 219.
[8] Nes and Mosettig, *J. Org. Chem.*, 1953, **18**, 276.
[9] Robins and Walker, *J.*, 1954, 3960.
[10] Ruzicka, Rudowski, Norymberski, and Jeger, *Helv. Chim. Acta*, 1946, **29**, 210.
[11] Brown, Brewster, and Schechter, *J. Amer. Chem. Soc.*, 1954, **76**, 467.
[12] Chavanne and de Vogel, *Bull. Soc. chim. Belg.*, 1928, **37**, 142.
[13] Skraup and Binder, *Ber.*, 1929, **62**, 1135.
[14] Taft, Levy, Aaron, and Hammett, *J. Amer. Chem. Soc.*, 1952, **74**, 4735.
[15] Bartlett and Barley, *ibid.*, 1938, **60**, 2416.
[16] Meerwein, *Annalen*, 1914, **405**, 156.
[17] Eisenlohr, *Chem. Zentr.*, 1926, **1**, 75.
[18] Zelinskii and Arbuzov, *Chem. Abs.*, 1940, **34**, 2696; Ohta, *ibid.*, 1950, **44**, 9226 (isomerisation of *cyclo*hexene to 1-methyl*cyclo*pentene).
[19] Tatevosyan, Melikyan, and Terzyan, *ibid.*, 1948, **42**, 1570 (dehydration of 1-*cyclo*butylethanol to 1-methyl*cyclo*pentene).
[20] Wallach and Fleischer, *Annalen*, 1907, **353**, 307.
[21] Wallach, *ibid.*, 1906, **347**, 325.
[22] Vogel, *J.*, 1938, 1323.
[23] Arnold, Amidon, and Dodson, *J. Amer. Chem. Soc.*, 1950, **72**, 2871.
[24] van der Bij and Kooyhan, *Rec. Trav. chim.*, 1952, **71**, 837.

the formation of the endocyclic isomer. Evidence for the greater stability of 1-methyl*cyclo*pentene has been given by Turner and Garner.[24a]



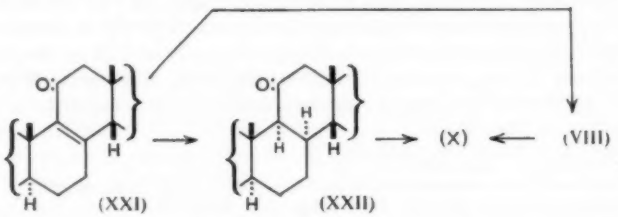
8α-*Steroids*. The 8α-Δ⁹-steroid (VII) was prepared from the 8α-11-ketone[4] (XVIII): 8α-ergostanol series). The preferred conformation of an 8α-steroid has been discussed;[25] ring B is a boat and ring C a chair conformation, the general appearance of the steroid still being approximately flat as in an 8β-compound. It was not surprising therefore that reactions at $C_{(11)}$ of the 8α-compounds resembled closely those of the related 8β-compounds. Thus reduction by lithium aluminium hydride of the 11-ketone afforded the 11β-alcohol (XIX; β-OH) in excellent yield, and reduction with sodium–propanol gave the equatorial 11-alcohol (XIX; α-OH) in high yield. However, acetylation of the 11α-hydroxyl group was more difficult than in the 8β-series, a 3β-monoacetate being isolated from either the 3β : 11α- or 3β : 11β-diol under the usual conditions of room temperature.

Dehydration of either of these monoacetates by phosphorus oxychloride in pyridine gave the Δ⁹-olefin (VII), the yield, as expected, being better from the axial 11β-alcohol.



In the 8β-series both 11-alcohols also give the corresponding Δ⁹-compound.[26] The Δ⁹-compound showed an absorption band at 818 cm.$^{-1}$ characteristic of a trisubstituted olefin.[27] With monoperphthalic acid it afforded an epoxide of probable α-configuration. Wolff–Kishner reduction of the 11-ketone (XVIII), which does not form carbonyl derivatives at room temperature, gave the deoxy-compound (XX).

14β-*Steroids*. In this series the starting material was the conjugated ketone (XXI), conveniently prepared from the isomeric Δ⁷-9β-compound by treatment with alkali.

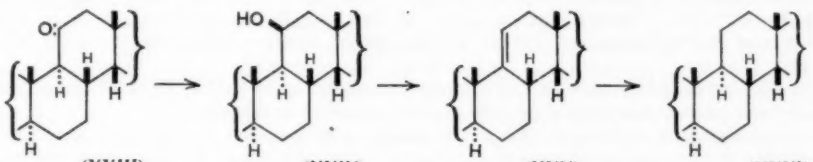


Hydrogenation afforded a saturated ketone, the 8α : 9α-configuration (XXII) of which is suggested by analogy with the steric course of the similar hydrogenation of the 14α-compound,[4] and by conformational arguments.[29] The saturated ketone (XXII), which did not yield a 2 : 4-dinitrophenylhydrazone under normal conditions, was reduced by the Wolff–Kishner method to the deoxy-compound (X). This was identical with the product

[24a] Turner and Garner, *J. Amer. Chem. Soc.*, 1957, **79**, 253.
[25] Clayton, Henbest, and Jones, *J.*, 1953, 2015.
[26] Crawshaw, Henbest, and Jones, *J.*, 1954, 731.
[27] Bladon, Fabian, Henbest, Koch, and Wood, *J.*, 1951, 2402.
[28] Sondheimer, Yashin, Rosenkranz, and Djerassi, *J. Amer. Chem. Soc.*, 1952, **74**, 2696.
[29] Djerassi, Frick, Rosenkranz, and Sondheimer, *ibid.*, 1953, **75**, 3496.

obtained from hydrogenation of the 7 : 9-diene (VIII); the steric course of the hydrogenation was thus established. The 7 : 9-diene (VIII) was obtained by reduction of the conjugated ketone (XXI) with lithium aluminium hydride followed by dehydration of the resulting 11-alcohol with acetic acid. Dehydration with mineral acid gave a mixture of nuclear dienes.

Some further experiments in the 14β-series were directed towards the preparation and reduction of the Δ^9-compound (XXV). Reduction with lithium and ammonia of the conjugated ketone (XXI) gave an 8β : 9α-dihydro-11-ketone (XXIII), the configuration being assigned by analogy with a similar reduction described in the sapogenin series, where the product was degraded to a compound of known stereochemistry.[20] Reduction of the 11-ketone (XXIII) by lithium aluminium hydride, followed by acetylation, afforded a 3-acetoxy-11-alcohol (XXIV). Evidence for an axial β-configuration for the 11-hydroxyl group in (XXIV) was provided by ready dehydration by hydrochloric acid in acetic acid: in the 14α-series where ring C has the same conformation this mixture of acids is known to convert 11α-alcohols into acetates and 11β-alcohols into olefins.[31,32] However, the new olefin was not the Δ^9-compound (XXV), which was prepared by treating the 11-alcohol (XXIV) with phosphorus oxychloride in pyridine. The Δ^9-compound thus obtained showed absorption bands in the infrared region assignable to a trisubstituted bond.[27] Acid converted the Δ^9-compound into the olefin obtained previously, and this was finally assigned a $\Delta^{8(14)}$-structure on the basis of end-absorption measurements.[33] In



(XXIII) (XXIV) (XXV) (XXVI)

this rearrangement catalysed by mineral acid, conformational driving force in the $\Delta^9 \longrightarrow \Delta^8$ stage arises from the greater stability of an olefinic bond in the latter position relative to the *cis*-C/D ring fusion. As the Δ^8-bond still contains a degree of instability from being in an unfavourable position in relation to the *trans*-A/B ring junction, further isomerisation to the more stable $\Delta^{8(14)}$-olefin takes place (cf. the rearrangement of cholest-8-en-3β-ol to its $\Delta^{8(14)}$ isomer catalysed by hydrogen chloride [34]).

The first ($\Delta^9 \longrightarrow \Delta^8$) stage suggests that the latter olefin is the more stable. If the steric situation during hydrogenation allowed β-approach of catalyst to the Δ^9-8β-system isomerisation to the Δ^8-compound should (initially) occur. Actually addition of hydrogen takes place, the reaction being envisaged as proceeding on the α-face to give 14β-ergostanol (XXVI). These reactions in the 14β-series proceed therefore very similarly to those with 14α-steroids, except that there is probably more driving force for the $\Delta^9 \longrightarrow \Delta^8$ rearrangement in the new series.

Experimental

In this and the following paper rotations were determined in chloroform and ultraviolet absorption in ethanol solutions.

3β-*Acetoxy*-8α-*ergostan*-11-*one* (XVIII).—A solution of 3β-acetoxyergosta-8 : 22-dien-11-one (2·5 g.) in ethanol (150 c.c.) was shaken with hydrogen in the presence of palladium–charcoal (4%; 2 g.) until a sample of product showed an ε_{2550} value <300; the uptake of hydrogen was

[30] Djerassi and Thomas, *Chem. and Ind.*, 1954, 1228.
[31] Bernstein, Lenhard, and Williams, *J. Org. Chem.*, 1954, **19**, 41.
[32] Crawshaw, Henbest, Jones, and Wagland, *J.*, 1955, 3420.
[33] Bladon, Henbest, and Wood, *J.*, 1952, 2737.
[34] Wieland and Görnhardt, *Annalen*, 1946, **557**, 248.

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then about 2·7 mol. The product was chromatographed on alumina (60 g.). Elution with benzene–light petroleum (100 c.c.; 1 : 4) gave 3β-acetoxyergost-8(14)-ene, m. p. and mixed m. p. 108°. Elution with benzene and crystallisation of the product from methanol gave the 11-ketone (0·51 g.), m. p. 163—164°, $[\alpha]_D$ −10·5°. Alkaline hydrolysis of the acetate gave 3β-*hydroxy*-8α-*ergostan*-11-*one*, m. p. 151—154°, $[\alpha]_D$ −33° (Found: C, 79·0; H, 11·4. $C_{28}H_{46}O_2,\frac{1}{2}H_2O$ requires C, 79·1; H, 11·5%).

8α-*Ergostane*-3β : 11β-*diol* (XIX; β-OH).—The 11-ketone (72 mg.) and lithium aluminium hydride (50 mg.) in ether (20 c.c.) were heated under reflux for 45 min. Crystallisation of the product from acetone yielded the 3β : 11β-*diol* (62 mg.), m. p. 195—198°, $[\alpha]_D$ −14° (Found: C, 80·05; H, 12·0. $C_{28}H_{50}O_2$ requires C, 80·3; H, 12·0%).

Acetylation of this diol with acetic anhydride–pyridine at 20° overnight gave, after crystallisation from aqueous acetone, the 3β-*monoacetate*, m. p. 175—178°, $[\alpha]_D$ +10° (Found: C, 78·25; H, 11·4. $C_{30}H_{52}O_3$ requires C, 78·2; H, 11·4%).

8α-*Ergostane*-3β : 11α-*diol* (XIX; α-OH).—Sodium (2 g.) was added during 30 min. to a boiling solution of 3β-acetoxy-8α-ergostan-11-one (0·2 g.) in propanol (50 c.c.). When the metal had dissolved the propanol was distilled off and the steroid isolated with ether. Crystallisation from aqueous acetone gave the 3β : 11α-*diol* (0·17 g.) as needles, m. p. 203—205°, $[\alpha]_D$ −46° (Found: C, 78·3; H, 11·9. $C_{28}H_{50}O_2,\frac{1}{2}H_2O$ requires C, 78·6; H, 12·0%). Acetylation of the diol as before yielded the 3β-*acetate*, m. p. 187—190°, $[\alpha]_D$ −65° (Found: C, 78·4; H, 11·65. $C_{30}H_{52}O_3$ requires C, 78·2; H, 11·4%).

3β-*Acetoxy*-8α-*ergost*-9-*ene* (VII).—(*a*) Phosphorus oxychloride (0·9 c.c.) was added to 3β-acetoxy-8α-ergostan-11β-ol (0·19 g.) in pyridine (7·5 c.c.) containing a drop of water. Crystallisation of the product from acetone gave 3β-*acetoxy*-8α-*ergost*-9-*ene* (0·11 g.) as needles, m. p. 88—92°, $[\alpha]_D$ +108° (Found: C, 81·1; H, 11·4. $C_{30}H_{50}O_2$ requires C, 81·4; H, 11·4%). Addition of *N*-ethylpiperidine (1 c.c.) to the initial mixture improved the yield from 60 to 85%.

(*b*) Similar dehydration of the 3β-acetoxy-11α-alcohol gave a 35% yield of 3β-acetoxy-8α ergost-9-ene, chromatographic purification being necessary in this case.

Hydrogenation of 3β-*Acetoxy*-8α-*ergost*-9-*ene*.—The steroid (84 mg.) in acetic acid (20 c.c.) was shaken in hydrogen in the presence of Adams's catalyst (75 mg.) for 3 hr.; no hydrogen was absorbed. Crystallisation from aqueous acetone yielded 3β-acetoxyergost-8(14)-ene (79 mg.), m. p. and mixed m. p. 107—109°.

Epoxidation of 3β-*Acetoxy*-8α-*ergost*-9-*ene*.—The olefin (0·6 g.) dissolved in dry ether (50 c.c.) was treated with monoperphthalic acid (2 mol.) in ether, the mixture then being kept at 25° for 2 days. Isolation of the steroid with ether followed by crystallisation from methanol yielded the 9α : 11α-*epoxide*, m. p. 132—134°, $[\alpha]_D$ +18·5° (Found: C, 78·7; H, 11·1. $C_{30}H_{50}O_3$ requires C, 78·55; H, 11·0%).

8α-*Ergostan*-3β-*ol* (XX).—A mixture of 3β-acetoxy-8α-ergostan-11-one (167 mg.), hydrazine hydrate (2 c.c.; 90%), and sodium methoxide in methanol (5 c.c.; 10%) was heated in a sealed tube at 170° for 20 hr. and then at 205° for 24 hr. Crystallisation of the product from aqueous methanol gave 8α-*ergostan*-3β-*ol* (118 mg.) as plates, m. p. 123—126°, $[\alpha]_D$ +43° (Found: C, 83·65; H, 12·55. $C_{28}H_{50}O$ requires C, 83·5; H, 12·5%).

Preparation of 3β-*Hydroxy*-14β-*ergosta*-7 : 9 : 22-*triene* (VIII).—Potassium hydroxide (20 g.) in water (20 c.c.) was added to boiling 3β-acetoxy-11-oxo-9β-ergosta-7 : 22-diene (15 g.) in ethanol (200 c.c.) under nitrogen. The solution was then heated under reflux for 4 hr. under nitrogen, and the steroid isolated with ether. Acetylation followed by crystallisation from methanol afforded 3β-*acetoxy*-11-*oxo*-14β-*ergosta*-8 : 22-*diene* (12·5 g.) as needles, m. p. 110—113°. The pure compound had m. p. 113—115°, $[\alpha]_D$ +117° (Found: C, 79·2; H, 10·15. $C_{30}H_{46}O_3$ requires C, 79·2; H, 10·2%). This compound was also prepared by similar treatment of the corresponding 9α-unconjugated ketone or 14α-conjugated ketone.

Solutions of the ketone (6·64 g.) in dry ether (100 c.c.) and lithium aluminium hydride (2·72 g.) in dry ether (400 c.c.) were mixed and then heated under reflux for 4 hr. The product, isolated with ether, showed no selective absorption in the 2400 Å region. The product was heated in acetic acid (50 c.c.)–acetic anhydride (50 c.c.) for 1 hr. on the steam-bath. Isolation with ether afforded 3β-*acetoxy*-14β-*ergosta*-7 : 9 : 22-*triene* (VIII), m. p. 63—64° (from methanol), $[\alpha]_D$ −30° (Found: C, 82·0; H, 10·85. $C_{30}H_{46}O_2$ requires C, 82·1; H, 10·6%). The corresponding *alcohol* had m. p. 117—120° (from methanol), $[\alpha]_D$ −39° (Found: C, 84·7; H, 11·2. $C_{28}H_{44}O$ requires C, 84·8; H, 11·2%). Ultraviolet absorption: $\lambda_{max.}$ 2400 Å (ε 16,100).

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8α : 14β-*Ergostanol* (1X).—(*a*) The foregoing trien-3β-ol (0·1 g.) in acetic acid (6 c.c.) was shaken in hydrogen with Adams's catalyst (0·1 g.) for 1 hr. Filtration and evaporation under reduced pressure and crystallisation from methanol gave **8α : 14β-*ergostanol*** as needles, m. p. 98—101°, $[\alpha]_D$ +33° (Found : C, 83·3; H, 12·4. $C_{28}H_{50}O$ requires C, 83·5; H, 12·5%). The ergostanol showed negligible absorption in the 2000—2200 Å region, and gave no colour with tetranitromethane.

(*b*) Sodium (1·9 g.) was dissolved in methanol (20 c.c.), 3β-acetoxy-8α : 14β-ergostan-11-one (0·17 g.) and hydrazine hydrate (90%; 9 c.c.) were added, and the solution was heated at 200° for 48 hr. in a steel autoclave. Several crystallisations of the product from methanol gave 8α : 14β-ergostanol (37 mg.) as needles, m. p. and mixed m. p. 98—101°, $[\alpha]_D$ +32°.

Oxidation of the alcohol by chromic acid–acetone [28] gave **8α : 14β-*ergostanone***, m. p. 97—99° (from methanol), $[\alpha]_D$ +51° (Found : C, 84·2; H, 12·1. $C_{28}H_{48}O$ requires C, 83·9; H, 12·1%). Reduction with sodium borohydride in aqueous dioxan gave back 8α : 14β-ergostanol, m. p. 99—100°.

3β-*Acetoxy*-8α : 14β-*ergostan*-11-*one* (XXII).—3β-Acetoxy-11-oxo-14β-ergosta-8 : 22-diene (2 g.) in ethanol (100 c.c.; freshly distilled from potassium hydroxide) was shaken with hydrogen in the presence of 5% palladised charcoal (1·3 g.). After 16 hr. the reaction was almost complete (light absorption). Chromatographic purification of the product afforded the ***ketone*** (1·1 g.), m. p. 71—74° (from methanol), $[\alpha]_D$ +60° (Found : C, 78·45; H, 11·25. $C_{30}H_{50}O_3$ requires C, 78·55; H, 11·0%). The infrared spectrum confirmed the presence of acetate and 11-ketone groups. Treatment overnight with boiling ethanolic potash, followed by reacetylation, gave back starting material.

3β-*Acetoxy*-11-*oxo*-14β-*ergost*-22-*ene* (XXIII).—3β-Acetoxy-11-oxo-14β-ergosta-8 : 22-diene (4·4 g.) in dry ether (50 c.c.) was run with stirring into lithium (0·25 g.) in liquid ammonia (250 c.c.). As the blue colour had then disappeared more lithium was added with stirring until it persisted. Ammonium chloride (5 g.) was added and the steroid isolated with ether and then acetylated. Chromatographic purification yielded the **11-*ketone*** (2·0 g.) (needles from methanol), m. p. 91—94°, $[\alpha]_D$ +38° (Found : C, 78·6; H, 10·55. $C_{30}H_{46}O_3$ requires C, 78·9; H, 10·6%). The compound showed no high-intensity absorption in the near-ultraviolet region. It was unchanged after vigorous treatment with alkali followed by reacetylation.

3β-*Acetoxy*-14β-*ergosta*-9 : 22-*diene* (XXV).—The foregoing ketone (1 g.) in dry ether was added to lithium aluminium hydride (1 g.) in ether (120 c.c.) and the mixture heated under reflux for 4 hr. The steroid was isolated with ether and acetylated overnight at 20° with acetic anhydride–pyridine, and the product crystallised from methanol, yielding the **11β-*alcohol*** (XXIV) (0·39 g.) as needles, m. p. 122—124°, $[\alpha]_D$ +38° (Found : C, 78·8; H, 10·9. $C_{30}H_{50}O_3$ requires C, 78·55; H, 11·0%). The infrared spectrum confirmed the presence of hydroxyl and acetate groups.

Phosphorus oxychloride (1 c.c.; freshly distilled from P_2O_5) was added to the 11-alcohol (0·15 g.) in dry pyridine (10 c.c.), and the mixture kept at 20° overnight. Crystallisation from methanol gave the **9 : 22-*diene*** (XXV) as needles, m. p. 61—63°, $[\alpha]_D$ +32° (Found : C, 81·65; H, 10·95. $C_{30}H_{48}O_2$ requires C, 81·8; H, 11·0%).

14β-*Ergostanol* (XXVI).—The 9 : 22-diene (70 mg.) in acetic acid (5 c.c.) was shaken with hydrogen and Adams's catalyst (50 mg.) until absorption ceased (1 hr.). The solution was filtered and evaporated to dryness, and the noncrystalline acetate hydrolysed with hot methanolic potash. Crystallisation from methanol gave **14β-*ergostanol*** (27 mg.) as needles, m. p. 114—116°, $[\alpha]_D$ +47° (Found : C, 83·5; H, 12·4. $C_{28}H_{50}O$ requires C, 83·5; H, 12·5%).

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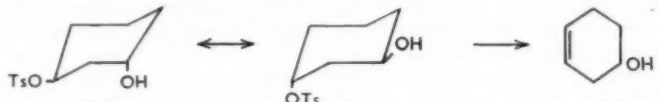
380. *Aspects of Stereochemistry. Part V.* Reactions of* cyclo*Hexane*-1 : 3-*diol Monoarenesulphonates with Alkali.*

By R. B. Clayton, H. B. Henbest, and Michael Smith.

At least four paths are available for the reaction of 1 : 3-diol monosulphonates with alkali. With monocyclic and steroid *cyclo*hexane-1 : 3-diol derivatives the course of the reaction is dependent on experimental conditions and the stereochemical arrangement of the reacting centres. Reasons are put forward for the exceptional formation of a 1 : 3-epoxy*cyclo*hexane system within a steroid molecule, and some of the reactions of this compound are described.

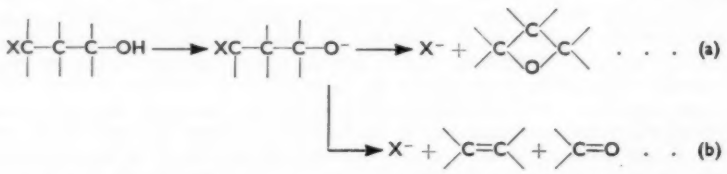
Before this work began no 1 : 3-epoxy*cyclo*alkane had been prepared. Cyclic epoxides are commonly produced by treatment of suitable halogenohydrins and related compounds with alkali: as a possible route to 1 : 3-epoxy*cyclo*hexane, *cyclo*hexane-*trans*-1 : 3-diol monotoluene-*p*-sulphonate (I) had earlier [1] been treated with sodium methoxide in methanol, but the only product obtained was *cyclo*hex-3-en-1-ol (II) in 80% yield. One



(IA) (IB) (II)

reason for the formation of the unsaturated alcohol could be a ready diaxial elimination of toluene-*p*-sulphonic acid from the less favourable conformation (IB) of the starting material. Consequently the reaction was re-investigated with a *trans*-diol monoester of the steroid series where ring inversion is impossible, and in this way a 1 : 3-epoxide was obtained [2] (see below).

To clarify subsequent discussion it may be noted that past and present results show that four types of reaction can take place between cyclic or acyclic 1 : 3-halogenohydrins and alkali. Two of these, epoxide formation (a) and fission into olefin and carbonyl compound [3] (b), depend on the formation of an intermediate anion,[4] whose powerful nucleophilicity provides the driving force for the intramolecular processes. [Conversely,



the fission of some 1 : 3-diols with strong acids [5] can be regarded as proceeding by a predominantly electrophilic process; the reaction may take place [6] *via* a transition state partaking of the character of the conjugate acid of the corresponding 1 : 3-epoxide.] For the intermediate anion, it will be shown that the choice between reaction paths (a) or (b)

* Part IV, preceding paper.

[1] Clarke and Owen, *J.*, 1950, 2103.

[2] Its preparation was first reported by Clayton and Henbest, *Chem. and Ind.*, 1953, 1315.

[3] This fission is one example of a more general carbon–carbon cleavage comprising reverse aldol, reverse Michael, etc., reactions: many examples, including the interesting fission of a 1 : 4-dihalide, have been collated by Grob and Baumann, *Helv. Chim. Acta*, 1955, **38**, 594.

[4] For some earlier observations with acyclic halogenohydrins, cf. Searles and Gortatowski, *J. Amer. Chem. Soc.*, 1953, **75**, 3030; Gaylord, Crowdle, Himmler, and Pepe, *ibid.*, 1954, **76**, 59.

[5] English and Brutcher, *ibid.*, 1952, **74**, 4279.

[6] Zimmerman and English, *ibid.*, 1954, **76**, 2294.

depends on its structure and stereochemistry, variation of the external conditions (including type of alkali used) being expected to have relatively little effect on this choice.

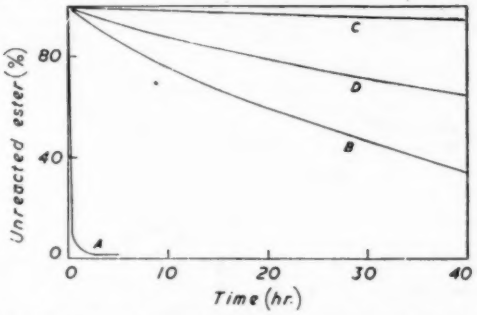
The other two reaction courses, elimination of acid (c_1 and c_2), and displacement of halide by a nucleophil (d), do not necessarily involve the hydroxyl group. As already mentioned, the elimination in *cyclo*hexane systems is more difficult when the sulphonic ester grouping is equatorial. Replacement (d) will be inhibited by steric factors such as increase of adjacent substitution and increased bulkiness of potential nucleophil.

On the other hand, reactions (a) and (b) should clearly be promoted by bases which efficiently generate the necessary intermediate anion. The formation of this anion by alkoxides in alcoholic solutions is an equilibrium process, which for given initial concentrations will be chiefly dependent on the relative acid strengths of the hydroxy-sulphonate and the solvent alcohol. As the acidities of alcohols decrease in the order primary, secondary, tertiary (p*K*'s of methyl, *iso*propyl, *tert.*-butyl alcohol, 16, 18, 19,

e.g.,

respectively [7]), a tertiary alkoxide in a tertiary alcohol should most completely generate the required anion of the starting material. It will be particularly disadvantageous to

*Reaction of toluene-*p*-sulphonates* (0·02M) *with alkali* (0·04M) *at* 50°. (*Unchanged ester was estimated spectrophotometrically; the pure ester has* $\lambda_{max.}$ 2250 Å; $\varepsilon = 12{,}700$.)



A, *Hydroxy-ester* (III) *and potassium* tert.*-butoxide in* tert.*-butyl alcohol.*
B, *Hydroxy-ester* (III) *and potassium methoxide in methyl alcohol.*
C, *Ester* (VIII) *and potassium* tert.*-butoxide in* tert.*-butyl alcohol.*
D, *Ester* (VIII) *and potassium methoxide in methyl alcohol.*

employ, for example, a primary alkoxide in a primary alcohol to produce an anion from a secondary (and even more so a tertiary) alcohol. The high yield of *cyclo*hexenol obtained previously from the monocyclic ester (I) by treatment with methoxide in methanol can be attributed to the non-formation of anion (see later) as well as to the possibility of conformational inversion to assist elimination.

Reactions of trans*-Hydroxy-sulphonates.*—(i) As an example of a compound with the ester grouping stabilised in an equatorial position, the steroid monotoluene-*p*-sulphonate (III) was prepared and treated in *tert.*-butyl alcohol with potassium *tert.*-butoxide (2 mol.). The reaction was rapid at 50° (Figure) with precipitation of potassium toluene-*p*-sulphonate: the only organic products identified were the crystalline 3α : 5α-epoxide (IV; 55%) and the liquid *seco*-ketone (V; 37%) [further reactions of all new steroid compounds are described towards the end of the paper]. By using a much larger amount of *tert.*-butoxide some 3α-*tert.*-butoxy-5α-alcohol (2%) was also obtained, the *cis*-disposition

[7] McEwen, *J. Amer. Chem. Soc.*, 1936, **58**, 1124.

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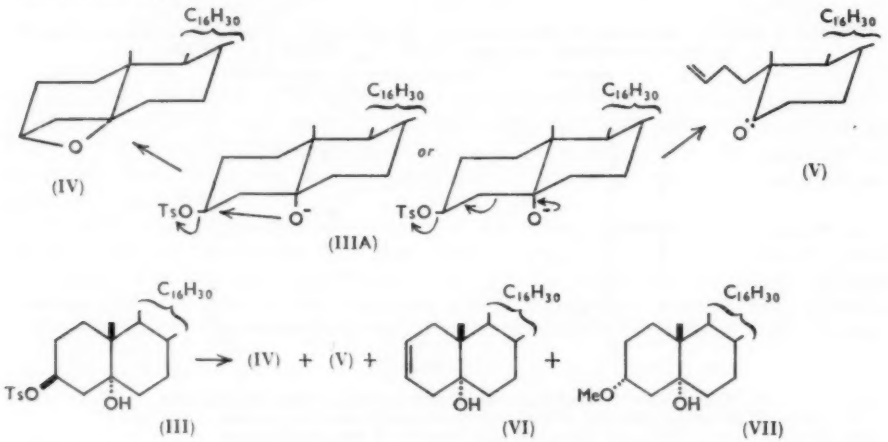
of groups being confirmed by the intramolecular hydrogen bonding revealed in the infrared spectrum.[8]

The reaction between the hydroxy-ester (III) [9] and potassium methoxide in methanol was much slower (Figure), giving a mixture of products corresponding to the four types of reactions (*a*)—(*d*). The greater rate of this reaction than that of the analogous 5-hydrogen compound under the same conditions (Figure) is due to the additional possibility of (rather inefficient) anion formation leading, as with the *tert.*-butoxide experiments, to the 3 : 5-epoxide and *seco*-ketone.

This discussion implies that the formation of epoxide and *seco*-ketone proceeds by first-order decomposition of the anion (IIIA), which is itself formed rapidly and reversibly from the starting materials :

$$\text{(III)} + \text{Bu}^t\text{O}^- \rightleftharpoons \text{Bu}^t\text{OH} + \text{(IIIA)} \longrightarrow \text{(IV)} + \text{(V)}$$

As *tert.*-butyl alcohol is the medium present in large excess, and as the acidity of the hydroxy-ester should only be comparable to that of this, the concentration of the intermediate anion will be small relative to the concentrations of hydroxy-ester and *tert.*-butoxide anion. As a close approximation, therefore, the reaction should be kinetically of the second order, the rate depending on [hydroxy-ester] and [Bu^tO^-]. This was the case for over 80% of the reaction.



Nace [10] has shown that the solvolysis of the 5α-hydrogen analogue (VIII) of the hydroxy-ester affords a mixture of olefin (see below) and 3α-methoxycholestane (X). As the rate of elimination from an equatorial toluene-*p*-sulphonate is essentially base-insensitive,[11] methanolysis of the hydroxy-ester (III) was performed in the expectation that the reactions of type (c) and (d) would now proceed with the exclusion of the reaction leading to epoxide and *seco*-ketone (the relatively weak base and nucleophil, sodium acetate, was added to buffer the solution against toluene-*p*-sulphonic acid produced in the reaction, 5α-hydroxy-steroids being dehydrated by acid). As expected, the experiment gave the hydroxy-olefin (VI) and methyl ether (VII), accompanied by a negligible amount

[8] Henbest and Lovell, *J.*, 1957, 1965.

[9] The corresponding methanesulphonates had earlier been treated with potassium hydroxide in methanol, *epi*cholesterol (25%) being isolated by an unspecified procedure; Plattner, Fürst, Koller, and Lang, *Helv. Chim. Acta*, 1948, **31**, 1455. No *epi*cholesterol could be detected in our product, and it seems likely that their material arose from the 3α : 5α-epoxide (22% in our experiment) during chromatography on alumina (see later).

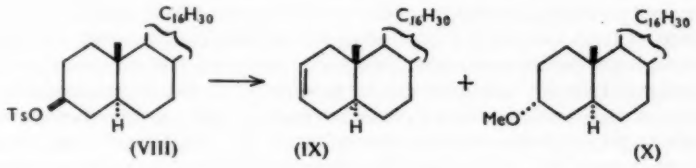
[10] Nace, *J. Amer. Chem. Soc.*, 1952, **74**, 5937.

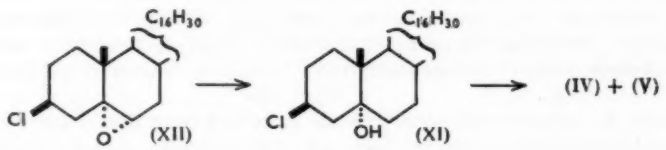
[11] Winstein and Holness, *ibid.*, 1955, **77**, 5562.

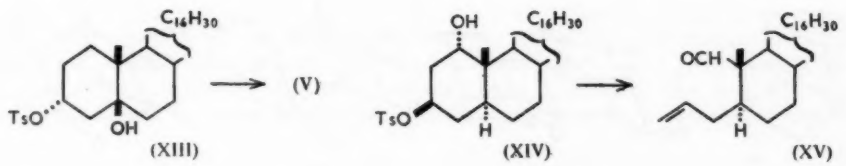
of *seco*-ketone and epoxide. [In contrast to the 5α-hydrogen series, the methoxy-compound (VII) is eluted before the accompanying olefin (VI) owing to chelation in the former compound.] A related hydrolysis took place when the hydroxy-ester was adsorbed on to active (but damp) alumina, the olefinic alcohol (VI) and cholestane-3α : 5α-diol being subsequently eluted.

The methanolysis of cholestanyl toluene-*p*-sulphonate carried out by Nace was repeated to give cholestene (25%) and 3α-methoxycholestane (75%) : the ether : olefin ratio is higher in the 5-hydrogen than in the 5-hydroxyl series owing to hindrance to α-approach of solvent imposed by the axial 5α-hydroxy-group. This experiment was repeated as it had been suggested that the olefin formed is a mixture of equal parts of cholest-2- and -3-ene. However, the optical rotation of the product (confirmed by us) was close to that of the pure Δ^2-olefin (IX) and, moreover, we could detect no cholest-3-ene in the mixture by infrared measurements.[12] Thus, there is little doubt that the formation of the olefin is thermodynamically controlled (as in the 5-hydroxy-series). As expected, alkaline solvolysis of the 5-hydrogen-ester (VIII) was much slower in *tert.*-butyl alcohol than in methyl alcohol (Figure).

As an example of a 5α-hydroxycholestane with a different $C_{(3)}$-equatorial group for heterolysis, the 3β-chloro-compound (XI) was prepared by lithium aluminium hydride reduction of the 5 : 6-epoxide (XII). The reaction of the chloro-alcohol with potassium *tert.*-butoxide was much slower than that of the sulphonate (in agreement with their







relative reactivities in simple S_N reactions); the epoxide and the *seco*-ketone were formed ultimately in the same proportion as before. With cholestane-3β : 5α-diol 3β-benzoate hydrolysis (regenerating diol) evidently proceeded rapidly relative to the formation of epoxide and *seco*-ketone, neither of which could be detected in the product.

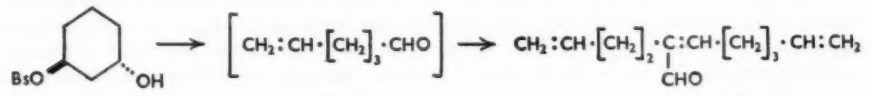
(ii) The hydroxy-ester (XIII) of the coprostane series was treated with potassium *tert.*-butoxide in *tert.*-butyl alcohol. No 3β : 5β-epoxide was formed, the product being the pure *seco*-ketone (V). The rate of the reaction was similar to that of its isomer (III).

[12] Henbest, Meakins, and Wood, *J.*, 1954, 800.

XUM

(iii) Partial esterification of the secondary alcohol, cholestane-1α : 3β-diol, with toluene-*p*-sulphonyl chloride gave a monoester [assumed to be (XIV); cf. acetylation of the diol [13]], which with potassium *tert.*-butoxide afforded the *seco*-aldehyde (XV) as sole product. The reaction was much quicker than those of the 5-hydroxy-compounds, probably owing to the more acidic secondary 1-hydroxyl group's giving rise to a greater concentration of intermediate anion.

(iv) After completion of these experiments with steroids, monocyclic compounds were again investigated. The reaction between *cyclo*hexane-*trans*-1 : 3-diol mono-*p*-bromobenzenesulphonate (XVI; Bs = benzenesulphonyl) and potassium *tert.*-butoxide was complete in 30 min. at 30°. The only identifiable product was a $C_{(12)}$-unsaturated carbonyl com-

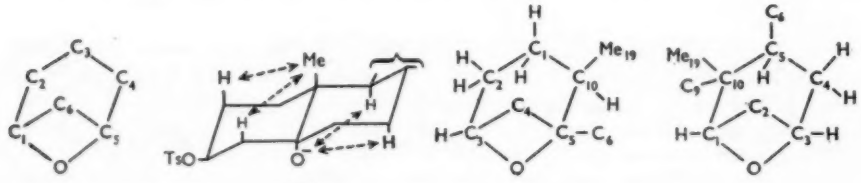


(XVI) (XVII) (XVIII)

pound, formulated as the aldehyde (XVIII) formed *via* aldol condensation of two molecules of the initial fission product (XVII) : condensation of *n*-butyraldehyde takes place under the same reaction conditions. No products as volatile as $C_{(6)}$-compounds (1 : 3-epoxy*cyclo*hexane or *cyclo*hex-3-en-1-ol) were detected by vapour-phase chromatography. Thus, as for the steroid disecondary compound (XIV), fission appears to be the only reaction taking place, the use of *tert.*-butoxide precluding formation of the *cyclo*hexenol obtained previously.

Thus, in reactions of types (a) and (b), proceeding *via* an intermediate anion, fission is the preferred reaction in the *cyclo*hexane series, an epoxide being (partially) formed in only one of the four systems studied. The difficulty in forming 1 : 3-epoxy*cyclo*hexanes may be due to the additional steric strains which have to be created : the four-membered oxide ring is approximately perpendicular to the remainder of the *cyclo*hexane ring which becomes altered so that atoms $C_{(1)}$ to $C_{(5)}$ (in XIX) become nearly coplanar and roughly in positions similar to those comprising a *cyclo*pentane ring. This distortion of the normal chair form of the *cyclo*hexane ring causes increased hydrogen eclipsing, especially in the $C_{(2)}$, $C_{(3)}$, and $C_{(4)}$ groups. Such eclipsing probably contributes largely to the greater heat of combustion per methylene group of *cyclo*pentane (158·7 kcal. mole^{-1}) than of *cyclo*hexane (157·4).[14]

It is left, therefore, to consider why some epoxide is formed from the hydroxy-ester (III). It is suggested that in this compound there are steric interactions of the solvated



(XIX) (XX) (XXI) (XXII)

(effectively large) oxygen atom and the angular methyl group with nearby axial CH groups (diagram XX), which help to force the $C_{(3)}$ atom towards the anion, thus assisting epoxide formation. The increased eclipsing in the region of $C_{(2)}$, $C_{(1)}$, and $C_{(10)}$ is counterbalanced by relief of strain during epoxide formation in the skew interactions indicated.

Although there are three skew interactions on the α-side of the coprostane hydroxy-ester (XIII) which might assist β-oxide formation, the bulky anion is now equatorial to

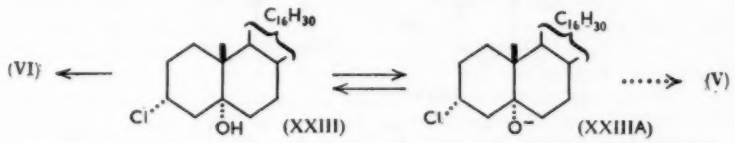
[13] Striebel and Tamm, *Helv. Chim. Acta*, 1954, **37**, 1094.
[14] Spitzer and Hofmann, *J. Amer. Chem. Soc.*, 1947, **69**, 211.

ring B and is only involved in one interaction (with the angular methyl group): these compressions are evidently not sufficient to promote oxide formation.

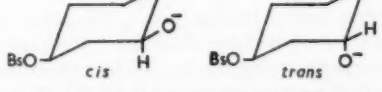
With the 1α-hydroxy-3β-ester (XIV) the interactions are very similar to those in the 5α-hydroxy-3β-ester (III) and yet no epoxide is produced. However, compared with either 5-hydroxy-compound, there is, with 1-hydroxy-ester, an additional factor preventing epoxide formation. Whereas in the linking of $C_{(3)}$ to the 5α-oxygen atom all the distortion is taken up in ring A (XXI), 1α : 3α-epoxide formation would involve simultaneous distortion of both linkages to ring B together with increased carbon eclipsing [$C_{(19)}$ methyl and $C_{(6)}$ methylene groups; see (XXII)].

The isolation of 3α : 5α-epoxycholestane is therefore probably exceptional as there are steric compressions sufficiently powerful to promote ring formation and yet the remainder of the molecule need not be greatly distorted. Formation of the 3α : 5α-epoxide may be compared with the ready solvolysis of cholesteryl toluene-*p*-sulphonate where participation of π-electrons from the 5 : 6-double bond can proceed to the extent of forming a covalent bond between $C_{(3)}$ and $C_{(5)}$.[15] In this reaction interactions between the angular methyl group and the axial hydrogen atom attached at $C_{(2)}$ and $C_{(4)}$ may again encourage movement of $C_{(3)}$ towards $C_{(5)}$ during the reaction. It would be interesting to carry out these reactions with steroids lacking the $C_{(19)}$ angular methyl group.

Stereochemistry of the Fission.—We have suggested [2] that the production of *seco*-ketone under such mild conditions from either of the 5-hydroxy-compounds (III) and (XIII) was a consequence of the parallel arrangement of the O–$C_{(3)}$ and the $C_{(4)}$–$C_{(5)}$ bond; this condition is also fulfilled in the *trans*-hydroxy-esters (XIV) and (XVI) where fission also occurs. The *cis*-chloro-alcohol (XXIII) with non-parallel Cl–$C_{(3)}$ and $C_{(4)}$–$C_{(5)}$ bonds was also treated with potassium *tert.*-butoxide. The only product isolated was cholest-2-en-5α-ol (VI), the infrared spectrum of the total product indicating that only a trace of *seco*-ketone was formed. It being assumed that some of the anion (XXIIIA) is generated under the experimental conditions, the result shows that fission does not occur when the bonds to be severed are in a (non-parallel) skew arrangement. The elimination observed was not especially rapid, its rate being similar to that of the conversion of the *trans*-isomer (XI) into epoxide and *seco*-ketone.



The rate of reaction of potassium *tert.*-butoxide with *cyclo*hexane-*cis*-1 : 3-diol mono-*p*-bromobenzenesulphonate was almost identical with that of the *trans*-isomer. Again the $C_{(12)}$ unsaturated aldehyde (XVIII) was obtained and no $C_{(6)}$-compounds were detected. For the fission the intermediate anions from the *cis*- and the *trans*-compound should be in the conformations shown (bonds to be broken being parallel).



The very close similarity between the two reactions shows that fission does not depend on the equatorial–axial arrangement of the bond to the anion. [Experiments with related acyclic hydroxy-esters will be reported later.]

Reactions of the New Steroid Compounds.—The 3α : 5α-epoxide (IV) with dilute acid

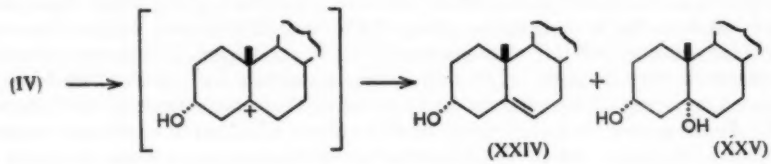
[15] Solvolysis of esters of the analogous 7β-hydroxy-Δ⁵-steroids leads to retention of configuraton at $C_{(7)}$ and no 5 : 7-*cyclo*steroid; cf. Shoppee, Summers, and Williams, *J.*, 1956, 1893.

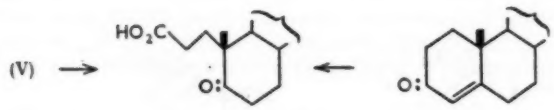
gave a mixture of *epi*cholesterol (XXIV) and the 3α : 5α-diol (XXV), both of which could arise *via* a $C_{(5)}$ carbonium ion. Retention of configuration at $C_{(5)}$ in the formation of the diol is noteworthy, as the hydration of epoxides usually gives *trans*-diols. However, retention of configuration has been observed [15] in the formation of 5α : 8α-epoxides from 5α : 8α-diols, and it appears that the intermediate carbonium ions in these reactions are sufficiently long-lived before reaction with an external or an internal nucleophil.

With boron trifluoride–ether complex in benzene the 3α : 5α-epoxide afforded a high yield of epicholesterol. Chromatographic alumina also seemed to act as a Lewis acid, for although the mixtures of epoxide and *seco*-ketone could be partially separated, isomerisation of the former to epicholesterol was very difficult to avoid. For the quantitative estimation of products, treatment with boron trifluoride followed by ready separation of *seco*-ketone and epicholesterol was used.

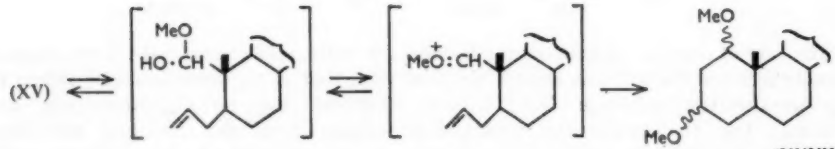
The epoxide was unaffected by boiling methanol containing potassium methoxide. It was not reduced by lithium aluminium hydride at room temperature, and this provided the basis for the most convenient method for isolating the pure epoxide, which could easily be separated by chromatography from the alcohol produced by reduction of the *seco*-ketone.

The structure of the *seco*-ketone was confirmed by its infrared absorption spectrum, by formation of a yellow 2 : 4-dinitrophenylhydrazone, and by ozonolysis to formaldehyde and the oxo-acid (XXVI), also produced [16] from cholest-4-en-3-one.





(XXVI)



(XXVII)

In contrast, the *seco*-aldehyde (XV) did not afford a dinitrophenylhydrazone in acidic methanol solution, being transformed instead into a colourless crystalline product, whose properties suggested a dimethoxycholestane structure : the same compound was produced in the absence of 2 : 4-dinitrophenylhydrazine. The colourless compound is probably one of the four possible 1 : 3-dimethoxy-compounds (XXVII) formed by a Prins reaction as suggested in the flow-chart. The non-formation of a 2 : 4-dinitrophenylhydrazone cannot be ascribed solely to hindrance imposed by the adjacent quaternary carbon group, as pivalaldehyde and pinacone readily give derivatives. Under the conditions wherein the presumed 1 : 3-dimethoxy-compound is formed, the *seco*-ketone (V) is almost

[15] Clayton, Henbest, and Jones, *J.*, 1953, 2015.

unaffected: ketones are generally less reactive than aldehydes, and the conformation of the alkyl side-chain in the *seco*-ketone may be less favourable for cyclisation than that in (XV).

From several of the experiments with the 5α-hydroxy-3-sulphonates an unsaturated alcohol with the same physical constants was obtained. This appears to be the pure Δ^2-5α-alcohol, and the presence of the Δ^3-5α-alcohol has not been detected. The structure is confirmed by (*a*) hydrogenation to cholestan-5α-ol, (*b*) formation of a single epoxide (2α : 3α) showing hydrogen bonding between the epoxy- and the hydroxy-groups, (*c*) lack of reactivity towards thionyl chloride under conditions where an allylic alcohol would be expected to give a chloro-compound (cf. conversion of a 5α-hydroxy-Δ^6-steroid into a 7α-chloro-Δ^5-compound [17]), and (*d*) optical-rotation evidence. As in the 5α-hydrogen series, elimination gives the more stable compound with the double bond opposite the bridge-head positions.

Experimental

Preparation of Sulphonic Esters.—cyclo*Hexane*-cis-1 : 3-*diol*. The diol (5 g.) and *p*-bromobenzenesulphonyl chloride (11 g.) were kept in pyridine (50 c.c.) at 0° for 24 hr. The product was isolated with chloroform, and then adsorbed from benzene–light petroleum (1 : 1; 250 c.c.) on to deactivated alumina (500 g.). Elution with the same solvent (1·5 l.) gave the *diester* (0·42 g.), needles (from ether), m. p. 115—117° (Found: C, 39·25; H, 3·3. $C_{18}H_{18}O_6S_2Br_2$ requires C, 39·0; H, 3·3%). Further elution with this mixture (0·5 l.) gave some oil (40 mg.), which was discarded. Elution with benzene–ether (1 : 1; 1 l.) afforded the *monoester* (12 g., 83%) as plates (from ether–light petroleum), m. p. 74—76° (Found: C, 42·8; H, 4·4. $C_{12}H_{15}O_4SBr$ requires C, 43·0; H, 4·5%).

cyclo*Hexane*-trans-1 : 3-*diol*. Similar treatment of the *trans*-diol gave the *diester* as plates (from ether), m. p. 154—155° (decomp.) (Found: C, 39·4; H, 3·4%), and the *monoester* (XVI), m. p. 60—61° (Found: C, 43·2; H, 4·6%).

Cholestane-3β : 5α-*diol*. The diol (1·7 g.) and toluene-*p*-sulphonyl chloride (1·7 g.) were kept in pyridine (20 c.c.) at 20° for 24 hr. The product was isolated with ether and chromatographed on deactivated alumina (100 g.). Elution with benzene afforded the ester (III) (2·3 g.) which crystallised from nitromethane as plates, m. p. 128—129° (decomp.), $[\alpha]_D$ −1° (Found: C, 73·2; H, 9·7. $C_{34}H_{54}O_4S$ requires C, 73·1; H, 9·75%). Ultraviolet absorption (in EtOH): $\lambda_{max.}$ 2250 Å; $\varepsilon = 12{,}700$. This compound was also obtained in a form with m. p. 143—145° (decomp.).

Cholestane-1α : 3β-*diol*. The diol (0·5 g.) and toluene-*p*-sulphonyl chloride (0·3 g.) were kept in pyridine (10 c.c.) at 20° for 24 hr. The product was isolated with ether, and then chromatographed on deactivated alumina (25 g.). Elution with benzene (200 c.c.) gave the 3β-*monoester* (XIV) (0·6 g., 85%) as prisms (from nitromethane), m. p. 135—137°, $[\alpha]_D$ +17·5° (Found: C, 73·4; H, 9·6. $C_{34}H_{54}O_4S$ requires C, 73·1; H, 9·75%). Ultraviolet absorption (in EtOH): $\lambda_{max.}$ 2250 Å; $\varepsilon = 12{,}000$.

Coprostane-3α : 5β-*diol*. The diol (1 g.) and toluene-*p*-sulphonyl chloride (1 g.) were kept in pyridine (5 c.c.) overnight at 20°. Isolation with and crystallisation from ether, gave the *ester* (XIII) (1·05 g., 75%) as prisms, m. p. 120—124°, $[\alpha]_D$ +36° (Found: C, 72·75; H, 9·55. $C_{34}H_{54}O_4S$ requires C, 73·1; H, 9·75%).

*Reaction of 5α-Hydroxycholestan-3β-yl Toluene-*p*-sulphonate* (III) *with Potassium* tert.-*Butoxide*.—Solutions of the ester (2 g.) in *tert.*-butyl alcohol (180 c.c.) and molar potassium *tert.*-butoxide (7 c.c.; 2 mol.) were mixed at 50° (potassium toluene-*p*-sulphonate began to precipitate almost immediately), and kept at 50° for 2 hr. The product (1·355 g., 98%) was isolated with ether.

One portion (0·41 g.) in dry benzene (25 c.c.) was treated with freshly distilled boron trifluoride–ether complex (0·5 c.c.) for 15 min. at 20° in order to isomerise the 3 : 5-epoxide to epicholesterol (see below). The product was isolated with ether and chromatographed on deactivated alumina (25 g.). Elution with light petroleum (200 c.c.) gave 4 : 5-seco*cholest*-3-*en*-5-*one* (V) (155 mg., 37%) as an oil, $[\alpha]_D$ +37°, n_D^{20} 1·5036 (Found: C, 83·65; H, 12·0. $C_{27}H_{46}O$ requires C, 83·85; H, 12·0%). Infrared absorption (in CS_2): bands at 1700 (ketone).

[17] Cf. Turner, *J. Amer. Chem. Soc.*, 1950, **72**, 579.

3040, 1637, and 910 cm.$^{-1}$ (vinyl group). Further elution of the chromatogram with ether (100 c.c.) gave *epi*cholesterol (220 mg., 53%) as plates (from methanol), m. p. 140—142°, $[\alpha]_D$ −37° (lit. values : m. p. 141·5°, $[\alpha]_D$ −35°).

The second portion (0·945 g.) in dry ether (50 c.c.) was treated with lithium aluminium hydride (150 mg.) for 30 min. at 20°. The product was isolated with ether and chromatographed on deactivated alumina (50 g.). Elution with light petroleum (300 c.c.) afforded **3α : 5α-*epoxycholestane*** (IV) (530 mg., 55%), as needles (from acetone), m. p. 82—86°, $[\alpha]_D$ +59° (Found : C, 84·0; H, 11·95. $C_{27}H_{46}O$ requires C, 83·85; H, 12·0%). This compound showed no appreciable absorption in the ultraviolet region; in the infrared region it showed a single strong band at 890 cm.$^{-1}$. Further elution of the chromatogram gave **4 : 5-*seco*cholest-3-en-5-ol** (380 mg., 39%) as a gum, which was dissolved in acetone (50 c.c.) and oxidised with 8N-chromic acid solution (0·5 c.c.) at 20° for 15 min. Isolation with ether and filtration through alumina afforded **4 : 5-*seco*cholest-3-en-5-one** (260 mg.), $[\alpha]_D$ +38°; the infrared spectrum was identical with that of the material obtained directly from the fission.

In an earlier experiment in which a much larger proportion of potassium *tert.*-butoxide was used, a small amount (2%) of **3α-tert.-*butoxycholestan*-5α-*ol*** was also isolated (by chromatography). This compound crystallised from methanol as needles, m. p. 94—95°, $[\alpha]_D$ +11° (Found : C, 80·5; H, 12·0. $C_{31}H_{56}O_2$ requires C, 80·8; H, 12·25%). The infrared absorption spectrum demonstrated the existence of chelation in the compound.

The *seco*-ketone (V) was characterised as its **2 : 4-*dinitrophenylhydrazone***, yellow needles (from ethanol), m. p. 145—150° (with change of form) (Found : C, 70·0; H, 9·0. $C_{33}H_{50}O_4N_4$ requires C, 69·95; H, 8·9%). Ultraviolet absorption (in EtOH) : $\lambda_{max.}$ 2640 Å; ε = 23,400.

Reactions of **3α : 5α-*Epoxycholestane*.**—Freshly distilled boron trifluoride–ether complex (0·1 g.) was added to the epoxide (1 g.) in dry benzene (10 c.c.), the resulting clear solution then being kept at 20° for 15 min. The product was isolated in the usual way and crystallised from methanol yielding *epi*cholesterol (XXIV) (0·8 g.) as plates, m. p. 141—143°, $[\alpha]_D$ −45° (Found : C, 84·1; H, 12·2. Calc. for $C_{27}H_{46}O$: C, 83·85; H, 12·0%). Acetylation gave *epi*cholesteryl acetate, m. p. 83—86°, $[\alpha]_D$ −12° (literature values for the alcohol, m. p. 141·5°, $[\alpha]_D$ −35° : for the acetate, m. p. 84—85°, $[\alpha]_D$ −12·5°).

The epoxide (125 mg.) in ethanol (8 c.c.) containing concentrated hydrochloric acid (50 mg.) was kept at 20° for 30 min. The product was isolated with ether and chromatographed on deactivated alumina (10 g.). Light petroleum eluted unchanged epoxide (40 mg.), m. p. 70—80° (impure). Light petroleum–benzene (9 : 1) eluted *epi*cholesterol (50 mg.), m. p. and mixed m. p. 140—142° (from methanol), $[\alpha]_D$ −43°. Ether–methanol (9 : 1) eluted **cholestane-3α : 5α-diol** (XXV) (20 mg.), flat needles (from ethyl acetate), m. p. 202—204°, $[\alpha]_D$ +16° (Found : C, 80·1; H, 11·8. Calc. for $C_{27}H_{48}O_2$: C, 80·15; H, 12·0%) (lit. values for the 3α : 5α-diol, m. p. 199°, $[\alpha]_D$ +17°).

Ozonolysis of the seco-*Ketone* (V).—The ketone (0·4 g.) in ethyl acetate (30 c.c.) was treated at −70° with a saturated (at −70°) solution of ozone in ethyl acetate until a slight blue colour persisted. The solution was shaken with ferrous sulphate solution, separated, and evaporated to give a gum that was dissolved in alcoholic ammoniacal silver nitrate solution and kept at 20° overnight. The acidic product (0·11 g.) was isolated with ether and crystallised from methanol to yield the oxo-acid (XXVI), m. p. 154·5—156°, $[\alpha]_D$ +35° (Found : C, 77·5; H, 11·0. Calc. for $C_{26}H_{44}O_3$: C, 77·2; H, 11·0%). A specimen prepared by ozonolysis of cholest-4-en-3-one had the same physical constants (including infrared spectrum).

In another experiment the ketone (0·28 g.) was dissolved in acetic acid (10 c.c.) and ozonised oxygen passed through the solution for 2 hr. The solution was steam-distilled into dimedone solution to yield the formaldehyde derivative (70 mg.), which after crystallisation from aqueous methanol had m. p. and mixed m. p. 192—193°.

Reaction of **5α-*Hydroxycholestan*-3β-*yl Toluene*-p-*sulphonate with Potassium Methoxide*.**—Solutions of the steroid (2·7 g.) in methanol (250 c.c.) and molar potassium methoxide solution (10 c.c.) were mixed and heated under reflux for 24 hr. The product was isolated with ether and chromatographed on alumina (200 g.). Elution with light petroleum–benzene (3 : 2; 800 c.c.) gave an oil (*A*) (455 mg.), $[\alpha]_D$ +40°, whose infrared spectrum indicated a mixture of the 3α : 5α-epoxide (IV) and the *seco*-ketone (V). Further elution with the same mixture afforded an oil (*B*) (73 mg.), $[\alpha]_D$ +25°, whose infrared spectrum indicated a mixture of *seco*-ketone and 3α-methoxycholestan-5α-ol. Elution with light petroleum–benzene (1 : 1; 1 l.) gave **3α-*methoxycholestan*-5α-*ol*** (VII) (540 mg.), needles (from aqueous acetone), m. p. 91—93°,

XUM

$[\alpha]_D$ +12·5° (Found: C, 80·5; H, 12·05. $C_{28}H_{50}O_2$ requires C, 80·3; H, 12·0%). Elution with benzene–ether (4 : 1; 1·2 l.) gave *cholest-2-en-5α-ol* (VI) (555 mg.), needles (from aqueous methanol), m. p. 93—95°, $[\alpha]_D$ +52° (Found: C, 83·8; H, 11·85. $C_{27}H_{46}O$ requires C, 83·9; H, 12·0%). Ether–methanol (49 : 1; 1 l.) eluted epicholesterol (150 mg.), m. p. 139—141°, $[\alpha]_D$ −38°. Fraction (*A*) was treated with boron trifluoride–ether complex in benzene and the product chromatographed, giving the *seco*-ketone (183 mg.) and *epi*cholesterol (260 mg.). The physical properties of fraction (*B*) showed that it was a mixture of equal amounts of the *seco*-ketone and the methoxy-alcohol. The yields of the four products are thus estimated to be: 3α : 5α-epoxide (22%), *seco*-ketone (12%), methoxy-alcohol (29%), and cholest-2-en-5α-ol (30%).

From the rotations of cholestane, cholestan-5α-ol, and cholest-2-ene, that of cholest-2-en-5α-ol can be estimated as about +52°, in good agreement with the value obtained. Further reactions of the unsaturated alcohol are given below.

Methanolysis of 5α-Hydroxycholestan-3β-yl Toluene-p-*sulphonate*.—The steroid (720 mg.) and potassium acetate (1 g.) were heated under reflux in methanol (100 c.c.) for 24 hr. The product was isolated with ether, and then chromatographed on alumina (50 g.). Elution with benzene (300 c.c.) gave 3α-methoxycholestan-5α-ol (150 mg.; 28%), needles (from acetone), m. p. 91—92°, $[\alpha]_D$ +13°. Elution with ether (450 c.c.) afforded cholest-2-en-5α-ol (240 mg.; 48%), m. p. 93—95°, $[\alpha]_D$ +53° (from aqueous methanol). The infrared spectrum of the reaction product showed that the 3α : 5α-epoxide and the *seco*-ketone had not been formed in any significant quantity.

Treatment of 5α-Hydroxycholestan-3β-yl Toluene-p-*sulphonate with Alumina*.—The steroid (1 g.) was adsorbed on active alumina (100 g.). Elution with benzene gave a small amount of oil (discarded). Benzene–ether (19 : 1; 1 l.) eluted cholest-2-en-5α-ol (0·4 g.; 58%), m. p. 93—95°, $[\alpha]_D$ +53° (from aqueous methanol). Elution with ether–methanol (49 : 1; 400 c.c.) gave cholestane-3α : 5α-diol (0·1 g.; 15%), m. p. 196—199°, $[\alpha]_D$ +19° (from aqueous methanol).

Reaction of 3β-Chlorocholestan-5α-ol with Potassium tert.-*Butoxide*.—M-Potassium *tert.*-butoxide (0·8 c.c., 2 mol.) was added to a solution of the steroid (156 mg.) in *tert.*-butyl alcohol (20 c.c.), the mixture being heated under reflux for 8 hr. The product was an oil (137 mg.; 96%) whose infrared spectrum showed it to be a mixture of the 3α : 5α-epoxide and the 4 : 5-*seco*-ketone in the same proportion as obtained from the toluene-*p*-sulphonate.

5α-Hydroxycholestan-3β-yl Benzoate.—Cholestane-3β : 5α-diol (0·5 mg.) was treated with benzoyl chloride (0·3 c.c.) in pyridine (10 c.c.) for 30 min. at 20°. The *benzoate* (0·54 g.) crystallised from methanol as needles, m. p. 157°, resolidifying to plates, m. p. 179°, $[\alpha]_D$ +14° (Found: C, 80·45; H, 10·3. $C_{34}H_{54}O_2$ requires C, 79·95; H, 10·7%). The benzoate (0·51 g.) in *tert.*-butyl alcohol (50 c.c.) was treated with M-potassium *tert.*-butoxide (2 c.c.), the mixture being heated under reflux for 3·5 hr. Isolation in the usual way gave cholestane-3β : 5α-diol (0·39 g.), m. p. 220—222°.

Reaction of 5β-Hydroxycoprostan-3α-yl Toluene-p-*sulphonate* (XIII) *with Potassium* tert.-*Butoxide*.—The reaction was carried out as described for the cholestane isomer, except that the reaction time was 1 hr. The product appeared to consist only of the *seco*-ketone (V), $[\alpha]_D$ +38°, with infrared absorption identical with those of previous pure samples. The same 2 : 4-dinitrophenylhydrazone was also prepared.

Reaction of 1α-Hydroxycholestan-3β-yl Toluene-p-*sulphonate* (XIV) *with Potassium* tert.-*Butoxide*.—The steroid (0·28 g.) in *tert.*-butyl alcohol (25 c.c.) was treated with M-*tert.*-butoxide (1 c.c.) for 30 min. at 50°. Isolation in the usual way gave 1 : 2-seco*cholest-2-en*-1-*al* (0·19 g.; 98%) as an oil, $[\alpha]_D$ +16°. This was adsorbed on neutral alumina and eluted with light petroleum: the infrared spectra (in CS_2) of successive fractions were identical with that of the crude material, with peaks at 2655 and 1715 (aldehyde), 3050, 1635, 990, and 910 cm.$^{-1}$ (vinyl group). A satisfactory analysis was not obtained on the small sample available (Found: C, 82·4; H, 11·8. $C_{27}H_{46}O$ requires C, 83·9; H, 12·0%). Treatment of the aldehyde with a 5% solution of sulphuric acid in methanol at 20° for 24 hr. gave a *compound* (probably a 1 : 3-dimethoxycholestane), m. p. 70—75°, $[\alpha]_D$ +23° (Found: C, 80·15; H, 11·85. $C_{29}H_{52}O_2$ requires C, 80·5; H, 12·1%). This compound gave no colour with tetranitromethane and showed no end absorption in the ultraviolet region. In the infrared region the compound showed a peak at 1090 cm.$^{-1}$, but no hydroxyl or carbonyl bands.

Methanolysis of Cholestan-3β-yl Toluene-p-*sulphonate* (VIII).—The steroid (0·2 g.) in dry methanol (25 c.c.) was heated under reflux for 72 hr., the product then being isolated and chromatographed on alumina. Pentane (20 c.c.) eluted cholest-2-ene (34 mg., 25%), m. p. 72—74°,

$[\alpha]_D$ +65° (from acetone). Further elution with pentane (50 c.c.) gave 3α-methoxycholestane (114 mg., 75%), m. p. 63—66°, $[\alpha]_D$ +20° (from acetone). The infrared spectrum of the hydrocarbon fraction gave no indication of cholest-3-ene. Pure cholest-2-ene has $[\alpha]_D$ +66°, pure cholest-3-ene $[\alpha]_D$ +56°.

Reaction of 3α-*Chlorocholestan-5α-ol* (XXIII) *with Potassium* tert.-*Butoxide*.—M-Potassium *tert.*-butoxide (2 c.c.) was added to the steroid (0·42 g.) in *tert.*-butyl alcohol (50 c.c.) and the mixture heated under reflux for 16 hr. The product (0·28 g.) was chromatographed on alumina (30 g.), the only crystalline product being cholest-2-en-5α-ol (0·21 g., 55%), m. p. and mixed m. p. 94—95°. The infrared spectrum of the total product showed the presence of only a trace of ketonic material.

Reactions of Cholest-2-en-5α-ol (VI).—*Hydrogenation*. The steroid (50 mg.) in ethyl acetate (10 c.c.) was shaken with hydrogen in the presence of Adams's catalyst (50 mg.) for 16 hr. Crystallisation of the product from aqueous methanol afforded cholestan-5α-ol, m. p. 101—103°, $[\alpha]_D$ +16°. This was identical with a sample (m. p. 101—103°; $[\alpha]_D$ +17°) prepared by reduction with lithium aluminium hydride of pure 5α : 6α-epoxycholestane.

Thionyl chloride. The steroid (47 mg.) in dry ether at 0° was treated with thionyl chloride (0·1 c.c.). The solution was kept at 20° for 1 hr., and the product, after crystallisation from acetone, gave starting material (33 mg.), m. p. and mixed m. p. 92—94°.

Peracid. Solutions of the steroid (0·34 g.) in dry ether (10 c.c.) and monoperphthalic acid in ether (3 c.c.; 1·2N-solution) were mixed and then kept at 20° for 3 hr. Crystallisation of the product from methanol afforded 2α : 3α-*epoxycholestan-5α-ol* (0·28 g.) as plates, m. p. 144—145°, $[\alpha]_D$ +32° (Found: C, 80·3; H, 11·45. $C_{27}H_{46}O_2$ requires C, 80·5; H, 11·5%). The position and intensity of the OH band at 3500 cm.$^{-1}$ were similar to those of peaks given by other 3α : 5α-dioxy-compounds.[8] Reduction of the epoxide with lithium aluminium hydride gave cholestane-3α : 5α-diol, m. p. and mixed m. p. 196—198°.

Reaction of cyclo*Hexane*-cis-1 : 3-*diol Mono*-p-*bromobenzenesulphonate with Alkali*.—M-Potassium *tert.*-butoxide (35 c.c., 2 mol.) was added to a solution of the ester (5·65 g.) in *tert.*-butyl alcohol (110 c.c.), and the pale yellow solution was then kept at 30° under nitrogen for 45 min. Isolation with ether gave a yellow oil [1·4 g.; 100% based on formation of (XVIII)], which was distilled at 10^{-4} mm.:

Fraction	Bath temp.	Wt. (mg.)	n_D^{21}	$E_{1\text{ cm.}}^{1\%}$ at 2290 Å
1	80°	200	1·4790	465
2	80—110	50	1·4850	400
3	110—115	500	1·4940	127
4	115—135	50	1·4962	—

There was a brown polymeric residue (*ca.* 0·5 g.). The declining intensities at $\lambda_{max.}$ (2290 Å in EtOH) were paralleled in the infrared region by a decrease in the intensities of the aldehyde bands (2700 and 1690 cm.$^{-1}$) relative to the vinyl bands (910 and 990 cm.$^{-1}$). The later fractions also showed an increasing amount of hydroxylic material (bands at 3530 and 3600 cm.$^{-1}$). [2-Ethylhex-2-en-1-al showed ultraviolet absorption (in pentane) $\lambda_{max.}$ 2250 Å (ε = 19,200).]

Fraction 1 was converted into the 2 : 4-*dinitrophenylhydrazone* which was purified chromatographically (0·25 g.) followed by several crystallisations from methanol, giving red needles, m. p. 115—116° (Found: C, 60·3; H, 6·4. $C_{18}H_{22}O_4N_4$ requires C, 60·3; H, 6·2%). Ultraviolet absorption (in $CHCl_3$): $\lambda_{max.}$ 3790 Å (ε = 29,200). The absorption of the derivative of the related 2-ethylhex-2-en-1-al has been given (in $CHCl_3$) as: $\lambda_{max.}$ 3850 Å (ε = 27,000).

Reaction of the trans-*Ester* (XVI) *with Alkali*.—Solutions of the ester (2 g.) in *tert.*-butyl alcohol (250 c.c.) and M-potassium *tert.*-butoxide (80 c.c., 2 mol.) were mixed and then kept at 30° under nitrogen for 45 min. Isolation with ether gave a yellow oil (2·7 g.; 95% based on formation of XVIII) which was fractionated at 10^{-4} mm. in 4 fractions, leaving much polymeric residue. Fraction 1 gave a good yield of the same 2 : 4-dinitrophenylhydrazone, m. p. 115—116°, as was obtained from the *cis*-ester. The infrared absorptions of each subsequent fraction were very similar to those of the corresponding fractions from the *cis*-ester.

Attempted Detection of C_6-*Compounds from the Hydroxy*cyclo*hexyl Bromobenzenesulphonates*.—A solution of each ester (40 mg.) in *tert.*-butyl alcohol (0·5 c.c.) was treated with M-potassium *tert.*-butoxide (0·15 c.c.; 2 mol.) at 20° for 1 hr. Potassium *p*-bromobenzenesulphonate quickly separated and the solution became lemon-yellow. Some of each solution was introduced into a vapour-phase chromatography unit with a column (temp. 118°) packed with Johns Manville

Celite 545 impregnated with di-*n*-nonyl phthalate. No C_6-compound could be detected in either reaction solution: the C_6-compounds present in a dilute solution of 1 : 2-epoxy*cyclo*hexane and *cyclo*hex-3-en-1-ol in *tert.*-butyl alcohol were readily detected by chromatography under these conditions.

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381. *Colour and Constitution. Part II.* The Effect of the Common Monatomic Substituents on the Ultraviolet Spectrum of Alternant Hydrocarbons.*

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The Hückel L.C.A.O. molecular-orbital theory is shown to provide a quantitative account of the bathochromic shifts observed in the ultraviolet spectrum of alternant hydrocarbons on the introduction of the common monatomic † substituents.

IN Part I,* the bathochromic shifts in the *p*-band ‡ of the ultraviolet spectrum which result from the introduction of a methyl group into an alternant hydrocarbon were discussed in terms of the Hückel L.C.A.O. molecular-orbital theory, and it was shown that a simple explanation of the origin and magnitude of these shifts is available. It is now of interest to examine how far this method is applicable to other common substituents. The available information on the effect of the common monatomic substituents (hydroxyl, methoxyl, amino, and the halogens) on the ultraviolet spectrum of alternant hydrocarbons, much of which is due to Jones [1] and to Friedel and Orchin,[2] is less complete that that for the methyl group, but is adequate for the present purpose.

While there is no difference from a theoretical viewpoint in the complexity of the problems of monatomic substituents and of the methyl group, in practice the former case is rather more difficult for several reasons. Monatomic substituents, particularly the amino-group, affect the ultraviolet spectrum to a greater degree, the bathochromic shifts being larger, and the general shape and fine structure of the *p*-band being often substantially or completely distorted. On occasion, when the bathochromic shift is very large, and the fine structure of the *p*-band of the parent hydrocarbon is completely absent in the derivative, the curves of the hydrocarbon and the derivative differ completely in appearance and no relation between them is apparent. This situation is fortunately rare and, where the bathochromic shift due to the substituent is small and the *p*-band of the derivative retains fine structure, there can be little doubt as to the close relation. Often, the larger the bathochromic shift, the more complete is the destruction in the derivative of both the fine structure and the general shape of the *p*-band. Several examples will be found below. A minor difficulty arises with large shifts in that their exact magnitude cannot be determined from the published curves. This is rarely serious as the estimate which can be made is usually of sufficient accuracy to test the predictions.

* Part I, *J.*, 1957, 646.

† Monatomic substituents are those contributing one *p*-orbital to the mesomeric system of the hydrocarbon.

‡ The nature and origin of the *p*-band are discussed in Part I.

[1] Jones, *J. Amer. Chem. Soc.*, (*a*) 1945, **67**, 2127; (*b*) 1941, **63**, 151; (*c*) 1940, **62**, 148; (*d*) *Chem. Revs.*, 1947, **41**, 353.

[2] Friedel and Orchin, "Ultraviolet Spectra of Aromatic Compounds," John Wiley and Sons, New York, 1951.

The nature of the hydrocarbon is also important in determining how far the spectrum of the derivative retains fine structure. Substituted anthracenes are particularly prone to this distortion of the *p*-band, the well-developed fine structure of the hydrocarbon being replaced by a smooth, broad curve whose centre can be estimated only roughly.

Another difficulty, related to the α-band, arises on occasion. In the hydrocarbon, the α-band is usually at longer wavelength and less intense than the *p*-band. These differences are often reduced or eliminated in the derivative, the α-band having nearly the same wavelength but greater intensity and the *p*-band being shifted bathochromically but being unchanged in intensity. In extreme cases, the two effects combine to produce a complete merging of the *p*- and the α-band.

In spite of these complications, the size of the shift resulting from the introduction of the substituent can usually be estimated from the published curves sufficiently accurately to test the theoretical method.

As with the methyl substituent, the shifts exhibit certain regularities. It is commonly accepted [3] that these substituents exert a bathochromic effect and the data collected in Table 2 substantiate this, although there are one or two cases in which one cannot be sure that a small hypsochromic shift is not occurring. No clear case of such a shift has been found, however, and the generalisation seems correct.

Method.—The effect of the monatomic substituents on the ultraviolet spectrum of alternant hydrocarbons has been discussed in terms of the simple Hückel L.C.A.O. molecular-orbital theory.[4] The introduction into the hydrocarbon of the single *p*-orbital of the substituent is regarded as a perturbation of the molecular orbitals of the former. It has been shown theoretically,[5] and supported by experimental evidence (cf. Part I and refs. 1*a* and 6), that the inductive effect of a substituent, represented by a change in the coulomb integral of the carbon atom to which it is attached, has little or no effect on the energy of the *p*-transition. The conjugative effect is dealt with by supposing that the result of the addition of the single *p*-orbital, of coulomb integral α, to the molecular orbitals of the hydrocarbon, is a perturbation of the latter orbitals. The resulting change in the energy of the *j*th molecular orbital ($\delta\varepsilon_j$) is given by the familiar expression of perturbation theory : [7]

$$\delta\varepsilon_j = \frac{c_{jr}^2}{\varepsilon_j - \alpha} \cdot \beta_{rs}^2 \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (1)$$

where c_{jr} is the atomic orbital coefficient of the *j*th molecular orbital at atom *r*, and β_{rs} is the resonance integral between the substituent(s) and the ring carbon atom (*r*). Applied to both the highest bonding (*i*) and the lowest antibonding molecular orbital of an alternant hydrocarbon, the change in energy (δE) of the *p*-transition is found to be :

$$\delta E = -c_{ir}^2 \cdot \beta_{rs}^2 \cdot 2\varepsilon_i/(\varepsilon_i^2 - \alpha^2) \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (2)$$

Since $\alpha^2 > \varepsilon_i^2 > 0$, and ε_i is a negative quantity, the shift is bathochromic. The usual values for the constants being inserted, the bathochromic shift ($\delta\lambda$ in mμ) is

$$\delta\lambda = 475 \cdot c_{ir}^2 \cdot \frac{1}{\varepsilon_i(\varepsilon_i^2 - \alpha^2)} \cdot (\beta_{rs}/\beta)^2 \quad . \quad . \quad . \quad . \quad . \quad . \quad (3)$$

where ε_i and α are expressed in units of β. β = 30,000 cal. per mole.

[3] Braude, *Ann. Reports*, 1945, **42**, 105.
[4] Pullman and Pullman, "Les Theories Electronique de la Chimie Organique," Masson et Cie, Paris, 1952; Dewar, "Progress in Organic Chemistry," Butterworths Scientific Publ., London, 1953, Vol. II, p. 1.
[5] Longuet-Higgins and Sowden, *J.*, 1952, 1404; Coulson, *Proc. Phys. Soc.*, 1952, **65**, *A*, 933.
[6] Epsztein, *Mém. Services chim. Etat*, 1951, **36**, 235.
[7] Coulson and Longuet-Higgins, *Proc. Roy. Soc.*, 1947, *A*, **191**, 39; Dewar, *J. Amer. Chem. Soc*, 1952, **74**, 3341.

TABLE 2. *Bathochromic shifts, resulting from the introduction of monatomic substituents, in the p-band.*

Posn. of subst.	λ (mμ) of parent	Shift (mμ) Calc.	Shift (mμ) Obs.	Ref.	Posn. of subst.	λ (mμ) of parent	Shift (mμ) Calc.	Shift (mμ) Obs.	Ref.
		(*a*) *Substituent*: OH and OMe					(*b*) *Substituent*: NH_2		
Naphthalene					Naphthalene				
1	276	17	13—17	2, *a*	1	276	36	30—40	*a*
2		6	0	2	2		14	5—10	*a*
Phenanthrene					Phenanthrene				
1	293	11	11—14	2	1	293	23	—	
2		0	0	2	2		0	0—1	6
3		9	—		3		20	30—35	6
4		5	—		4		11	—	
9		16	12—16	2	9		34	*ca.* 30	6
Pyrene *					Pyrene *				
1	333	10	13	2	1	333	18	—	
3		15	13, 17	1*a*, *b*	3		29	25—35	1*a*, *b*
4		0	2	1*a*, *b*	4		0	4	1*a*, *b*
Chrysene *					Anthracene				
1	319	6	7	*c*	1	339	21	—	
2		15	12	*c*	2		11	14	1*d*
3		9	16	*c*	9		43	*ca.* 50	*f*
4		1	0	*c*					
5		6	9	*c*					
6		6	15	*c*					
1 : 2-Benzanthracene					1 : 2-Benzanthracene				
3	341	10	Small	1*b*	3	341	18	Small	1*b*
9		18	11	*d*	8		20	30—50	1*a*
10		23	12	1*a*, 2	10		44	40—60	1*b*
4′		3	Small	*e*					
		(*c*) *Substituent*: Cl and Br					(*d*) *Substituent*: F		
Naphthalene					Naphthalene				
1	276	9	10, 11	*a*	1	276	5	5—6	*j*
2		3	3, 4	*a*	2		2	Small	*j*
Anthracene									
1	374	5	7, 8	*g*, *h*					
2		3	3	*h*					
9		11	10—12	*i*					
Naphthacene									
5	471	11	13, 14	*g*					
Phenanthrene					Phenanthrene				
1	293	6	—		1	293	3	3	*k*
2		0	1, 2	2	2		0	1·5	*k*
3		5	—		3		2·5	0	*k*
4		3	—		4		1·5	4	*k*
9		9	9	2	9		4·5	4	*k*
Pyrene *					Pyrene *				
3	333	7	10	*b*	1	333	3	4—5	*k*
1 : 2-Benzanthracene									
6	341	2	5—6	2					
10		11	14—15	*d*					

* Ring Index numbering.

Refs.: (*a*) de Laszlo, *Proc. Roy. Soc.*, 1926, *A*, **111**, 355. (*b*) Förster and Wagner, *Z. phys. Chem.*, 1937, **37**, *B*, 353. (*c*) Holiday and Jope, *Spectrochim. Acta*, 1950, **4**, 157. (*d*) Badger and Pearce, *J.*, 1950, 3072. (*e*) Holiday, *Cancer Res.*, 1943, **3**, 689. (*f*) Craig and Short, *J.*, 1945, 419. (*g*) Clar and Marschalk, *Bull. Soc. chim. France*, 1950, **17**, 433. (*h*) Conrad-Billroth, *Z. phys. Chem.*, 1936, **33**, *B*, 133. (*i*) Etienne and Le Grand, *Bull. Soc. chim. France*, 1953, **20**, 108. (*j*) Ferguson, *J.*, 1954, 304. (*k*) Bavin and Dewar, *J.*, 1955, 4486.

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When it is seen that equation (3) is identical with that derived for the methyl substituent, the close relation between the bathochromic effects of the two classes of substituents becomes clear. Within a given hydrocarbon, the factor determining the size of the bathochromic shift at any position is the atomic orbital coefficient of the top bonding molecular orbital at the ring carbon atom concerned, the energy term being constant.

In equation (3) there are two quantities which must be assigned for each substituent, the coulomb integral α, and β_{rs}/β. The values chosen for these terms are set out in Table 1.

TABLE 1.

Substituent	N	O	Cl	Br	F
Coulomb integral	$1{\cdot}0\beta$	$1{\cdot}3\beta$	$1{\cdot}0\beta$	$1{\cdot}0\beta$	$1{\cdot}5\beta$
β_{rs}/β	0·4	0·4	0·2	0·2	0·25

The choice of the coulomb integrals is governed by the accepted order of the electronegativities [8] and, as with the methyl substituent, the values of β_{rs}/β have been chosen to reproduce the α-naphthalene results. The resulting values are reasonable, and, in any case, no rational choice of these parameters would give results outisde of the correct order of magnitude.

The results calculated from equation (3) are compared with the available experimental data in Table 2.

DISCUSSION

The bathochromic shifts of the monatomic substituents are quite similar to those of the methyl group. In both instances, the *meso*-positions of anthracene and similar positions show large shifts, while the β-position of naphthalene and similar positions show small shifts. The identical expressions derived for both classes of substituents explain this position exactly. The differences in absolute magnitude arise from the differing coulomb integrals of the heteroatoms and from the differing resonance integrals between these atoms and the ring carbon atom.

Hydroxy- and Methoxy-substituents.—These groups give rise to very similar shifts. The methoxy-shifts seem slightly larger than the hydroxy-shifts, and this may be due to a reduction in the coulomb integral of the oxygen atom by the methyl group. The effect is quite small, however, and the groups are not distinguished further.

The bathochromic shifts in the *p*-band introduced by the hydroxy- or methoxy-group for naphthalene follow the generalisation just given. There is some distortion of the fine structure of the *p*-band in the 1-hydroxy-compound but almost none in the 2-hydroxy-derivative, in conformity with the previous statement that the greater the bathochromic shift, the greater the distortion. The ultraviolet spectra of the hydroxyanthracenes are unknown, but experimental data are available for three of the hydroxyphenanthrenes. The 1- and the 9-hydroxy-compound show considerable distortion of the fine structure and general shape of the *p*-band, but the shifts can be determined with sufficient accuracy to show the agreement with the calculations. In 2-hydroxyphenanthrene, the zero bathochromic shift is accompanied by excellent retention of the fine structure of the *p*-band.

A very small bathochromic shift and good retention of the fine structure are also shown by 4-hydroxypyrene, while 1- and 3-hydroxypyrene show larger shifts and there is concomitant distortion of the fine structure. The calculated and experimental shifts are again in good agreement.

The monomethoxychrysenes are remarkably free from distortion of the fine structure of the *p*-band. The steric bathochromic shift found in 6-methylchrysene occurs in 6-methoxychrysene. 3-Methoxychrysene also shows a larger bathochromic shift than the calculations suggest, but in the remaining four positions agreement is good.

In the monomethoxy-1 : 2-benzanthracenes, quantitative agreement between the

[8] Pauling, "The Nature of the Chemical Bond," Cornell Univ. Press, Ithaca, New York, 1945, p. 60.

calculated and experimental shifts is inferior to that found with the other hydrocarbons. The 9- and the 10-methoxy-compound show very severe distortion of the fine structure of the *p*-band.

The conversion of a phenol into its anion causes a bathochromic shift of the *p*-band.[1a, 2] This may be due either to an increase in the resonance integral of the bond between the oxygen atoms and the ring, or to a decrease in the coulomb integral of the oxygen atom. The latter interpretation is preferred since an increase in negative charge on an atom is commonly supposed to decrease the coulomb integral.[9]

The Amino-substituent.—This often causes very large shifts with severe distortion of the fine structure of the *p*-band and of the general appearance of the spectrum. Thus, in α-naphthylamine, the clear distinction of the *p*- and the α-band is lost and the bathochromic shifts cannot be estimated accurately. The spectrum of β-naphthylamine is less distorted and the shift is of the calculated size.

The published spectrum of 2-aminoanthracene is abnormal in that the fine structure of only one half of the *p*-band is destroyed, that of the short-wavelength portion being retained very well, undoubtedly because the intensified α-band emerges beneath the long-wavelength portion of the *p*-band. From the remaining fine structure, it is not possible to decide which of two vibrational peaks is derived from a given peak of the parent hydrocarbon. One assignment leads to a bathochromic shift of 14 mμ while the alternative is a hypsochromic shift of 3 mμ: the calculated shift of 11 mμ shows that the first alternative is correct. The spectrum of 9-aminoanthracene is very badly distorted but the bathochromic shift seems to be of the calculated size.

The calculated and experimental shifts of the known monoaminophenanthrenes agree satisfactorily; the inversion in the order of the shifts of the 3- and the 9-compound may be due to the rather bad distortion of the spectra and the resulting difficulty in estimating the shifts.

4-Aminopyrene exhibits a very small shift and excellent retention of the fine structure of the *p*-band, while the 3-compound shows a larger shift and substantial distortion of the fine structure. Both results agree well with the calculations.

Very severe distortion of the fine structure of the *p*-band of 8- and 10-amino-1 : 2-benzanthracene prevents an accurate estimate of their bathochromic shifts. The spectrum of 3-amino-1 : 2-benzanthracene exemplifies a situation which has been noted previously (Part I): the 3- and the 4-derivative are calculated to show quite large shifts, as would be expected from their relation to the 9- and 10-position of phenanthrene, but the experimental result is that 3-amino-1 : 2-benzanthracene shows a small shift.

The Halogen Substituent.—This causes rather small shifts, accompanied by very good retention of the fine structure of the *p*-band. There is good agreement between the experimental and the calculated results for naphthalene and for the known phenanthrenes. The ultraviolet spectra of all of the monofluorophenanthrenes have been recorded. In the phenanthrene ring, the 4-position is unreliable for comparison between theory and experiment owing to the probable intervention of steric effects. For three of the remaining four positions, there is good agreement between experimental and calculated values; the exception is the 3-position, where theory suggests a moderate shift but no shift is found in practice; there is no apparent explanation of this anomoly, and it would be of interest to examine the spectra of the other halogenophenanthrenes.

Other Substituents.—There seems no reason why the current method should not be extended to other, more complex substituents, and the literature has been surveyed with respect to the vinyl, carbonyl, and cyano-substituents. These naphthalene derivatives show the expected results, the bathochromic shifts of the *p*-band being several times greater in the 1- than in the 2-position,[2, 10] but data are scanty. More complex substituents containing four or more *p*-orbitals are in principle amenable to the method, but

[9] Bassett, Brown, and Penfold, *Chem. and Ind.*, 1956, 892 and refs. therein.
[10] Ref. *a* of Table 2.

the large size of their shifts, the extensive distortion of the fine structure of the *p*-band, and the increased arithmetical manipulation restrict the utility of the method.

It seems, then, that at least an approximate value is available for the bathochromic shifts due to the common monatomic substituents, in the ultraviolet spectra of alternant hydrocarbons. The method should prove of value in interpreting the spectrum of new compound of unknown orientation of the substituents.

The author is indebted to Professor M. J. S. Dewar for reading the manuscript and for advice and encouragement.

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382. *The Synthesis and Reactions of Branched-chain Hydrocarbons. Part XI.** 2 : 2 : 4 : 6 : 6-*Pentamethylhept-3-ene, One of the Constituents of Triisobutylene.*

By M. A. Davis and W. J. Hickinbottom.

Pyrolysis of the stearates of 2 : 2 : 4 : 6 : 6-pentamethylhepten-3-ol, 2 : 2 : 4-trimethylhexan-3-ol and 4-ethyl-2 : 2-dimethylhexan-3-ol gives the corresponding olefins without rearrangement or without migration of the double bond. The addition of some pyridine to the ester before pyrolysis was found to be necessary.

It has been established,[1] from examination of the products of ozonolysis and oxidation, that technical tri*iso*butylene is a mixture of four isomeric dodecenes (I—IV). The main constituents are (I) and (II), present in about equal amounts; (III) and (IV) together comprise about 10% of the technical product, although some wide variation in the relative proportions occurs. No satisfactory separation of any one constituent has yet been achieved by distillation. It has however been possible to isolate *as*-di*neo*pentylethylene (I) in a pure state by taking advantage of the fact that it is more resistant to oxidation than its isomers.[2] It is also reported that components (III) and (IV) can be separated from technical tri*iso*butylene by their more ready combination with hydrogen chloride.[3]

$(Me_3C\cdot CH_2)_2C{:}CH_2$ (I) $\quad Me_3C\cdot CH{:}CMe\cdot CH_2\cdot CMe_3$ (II) $\quad Me_3C\cdot CH_2\cdot CMe_2\cdot CH_2\cdot CMe{:}CH_2$ (III)

$Me_3C\cdot CH_2\cdot CMe_2\cdot CH{:}CMe_2$ (IV) $\quad Me_3C\cdot CH(OH)\cdot CHRR'$ (V)

For another investigation it was necessary to have a considerable quantity of 2 : 2 : 4 : 6 : 6-pentamethylhept-3-ene (II) in a pure state. A satisfactory method appeared to consist in the dehydration of 2 : 2 : 4 : 6 : 6-pentamethylheptan-3-ol (V; R = Me, R′ = $CH_2\cdot CMe_3$) by thermal decomposition of its carboxylic esters or its methylxanthate. It is known already that these methods can be applied successfully to the preparation of *tert.*-butylethylene from 3 : 3-dimethylbutan-2-ol without rearrangement of the sensitive *neo*pentyl group.[4] In the projected method of preparation of (II), bond migration is also possible. Accordingly preliminary experiments were carried out on simpler alcohols having the same structural features (V; R = Me, R′ = Et; or R = R′

* Part X, *J.*, 1956, 911.

[1] McCubbin, *J. Amer. Chem. Soc.*, 1931, **53**, 356; Whitmore *et al.*, *ibid.*, 1941, **63**, 2035, 2200.
[2] Bartlett, Frazer, and Woodward, *ibid.*, p. 495; Hickinbottom and Wood, *J.*, 1951, 1601.
[3] U.S.P. 2,485,265.
[4] Dolliver, Gresham, Kistiakowsky, and Vaughan, *J. Amer. Chem. Soc.*, 1937, **59**, 832; Stevens and Richmond, *ibid.*, 1941, **63**, 3135.

= Et). It was found that pyrolysis of the stearates of these alcohols gave the required olefins if some pyridine was added. If this were omitted, the product boiled over a range of several degrees and no steady refractive index could be obtained. The olefins (II) and that from (V; R = Me, R′ = Et) boiled over a range of 0·5—1·0° and the refractive index drifted about 0·0007—0·0010 unit. This variation can be reasonably attributed to the presence of *cis*- and *trans*-isomers, since only the expected fission products were obtained from ozonolysis; further support for this view is provided by the observation that from (V; R = R′ = Et), where there is no possibility of *cis-trans*-isomerism, the olefin was of almost constant b. p. and n_D^{20}.

Experimental

2 : 2 : 4 : 6 : 6-*Pentamethylhept*-3-*ene*.—2 : 2 : 4 : 6 : 6-Pentamethylheptan-3-ol was prepared essentially by the method of Whitmore *et al.*[5] from 2 : 4 : 4-trimethylpentanoyl chloride with an excess of *tert.*-butylmagnesium chloride; 379 g. of acid chloride gave 2 : 2 : 4 : 6 : 6-pentamethylheptan-3-ol (488 g.), b. p. 100—102°/21 mm., n_D^{20} 1·4420, and 2 : 2 : 4-trimethylpentan-1-ol (121 g.), b. p. 79—80°/23 mm., n_D^{20} 1·4285—1·4270.

2 : 2 : 4 : 6 : 6-Pentamethylheptan-3-ol (84 g.) was added, in one portion, to stearoyl chloride (from 142 g. of stearic acid and 60 g. of thionyl chloride) and heated in a steam-bath for 12 hr. Ethyl alcohol (5 g.) was then added and heating continued for 1 hr. and then under reduced pressure to remove volatile matter. The ester formed was diluted with ether (250 c.c.) and washed with water till neutral to litmus. A final washing with saturated sodium chloride solution helped to clear the heavy emulsion which had formed. The dried ether solution ($CaCl_2$) was concentrated under reduced pressure and then heated in a metal-bath at 360° for 1 hr. after addition of 2 c.c. of pyridine. The distillate was shaken with 20% aqueous sodium hydroxide, then treated with calcium chloride solution to precipitate all the stearic acid which had distilled over with the olefin. The crude olefin was isolated by steam-distillation. The crude hydrocarbon (37 g.) had b. p. 178—181°, n_D^{20} 1·4370—1·4380. Repetition on a 2-mole scale gave 172 g. of crude olefin, b. p. 178—181°. Further distillation gave pure 2 : 2 : 4 : 6 : 6-*pentamethylhept*-3-*ene*, b. p. 180·5°, n_D^{20} 1·4370 (Found: C, 85·7; H, 14·4. $C_{12}H_{24}$ requires C, 85·6; H, 14·4%).

Ozonolysis of the olefin in chloroform and treatment of the ozonide with water and 30% hydrogen peroxide gave trimethylacetic acid (anilide, m. p. and mixed m. p. 134°) and 4 : 4-dimethylpentan-2-one (2 : 4-dinitrophenylhydrazone, m. p. and mixed m. p. 99—100°), together with a small amount of trimethylacetaldehyde (2 : 4-dinitrophenylhydrazone, m. p. and mixed m. p. 210°).

The components of all mixtures of carbonyl compounds obtained in this work, from ozonolysis or by oxidative fission of glycols, were separated and identified as their 2 : 4-dinitrophenylhydrazones by chromatography on silica or alumina, with benzene–light petroleum for elution.

The olefin with perbenzoic acid in chloroform gave 3 : 4-*epoxy*-2 : 2 : 4 : 6 : 6-*pentamethylheptane*, b. p. 71°/12 mm., n_D^{20} 1·4308 (Found: C, 78·1; H, 13·0. $C_{12}H_{24}O$ requires C, 78·2; H, 13·1%). It is hydrated when shaken with cold dilute sulphuric acid, to the glycol and other products. The epoxide (2 g.) and 0·5% sulphuric acid (25 c.c.) after 20 hr. gave a viscid oil (0·3 g.). Its identity as 2 : 2 : 4 : 6 : 6-pentamethylheptane-3 : 4-diol was confirmed by oxidative fission to trimethylacetaldehyde and methyl *neo*pentyl ketone; no other carbonyl compound could be detected.

The epoxide, heated with aqueous-alcoholic 30% sulphuric acid containing 2 : 4-dinitrophenylhydrazine, gives the 2-*tert.*-butyl-2 : 4 : 4-trimethylpentanal 2 : 4-dinitrophenylhydrazone (not very good yield) as yellow needles, m. p. and mixed m. p. 152—153°.

2 : 2 : 4-*Trimethylhex*-3-*ene*.—The crude stearate of 2 : 2 : 4-trimethylhexan-3-ol [from the alcohol (72 g.) and stearoyl chloride (from 150 g. of stearic acid)] was heated at 360° for 4 hr. with pyridine (2 c.c.). The olefin, obtained in 56% yield, had b. p. 128°, n_D^{20} 1·4230. It was identified by ozonolysis to trimethylacetaldehyde and ethyl methyl ketone. No other carbonyl compound could be detected. When the stearate was pyrolysed without the addition of pyridine, the olefin had b. p. 128—132°, n_D^{20} 1·4226—1·4248. Whitmore and Laughlin [6]

[5] Whitmore *et al.*, *J. Amer. Chem. Soc.*, 1937, **59**, 643.
[6] Whitmore and Laughlin, *ibid.*, 1933, **55**, 3737.

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dehydrated 2 : 2 : 4-trimethylhexan-3-ol by heating it with naphthalene-2-sulphonic acid and obtained mixed 2 : 2 : 4-trimethylhex-3- and -4-ene, b. p. 128—130·2°, n_D^{20} 1·4220.

The olefin with benzoyl hydrogen peroxide in chloroform gives 3 : 4-*epoxy*-2 : 2 : 4-*trimethylhexane* (45%), b. p. 80—80·5°/77 mm., n_D^{20} 1·4170—1·4165 (Found: C, 75·8; H, 12·8. $C_9H_{18}O$ requires C, 76·0; H, 12·6%). There was also formed some higher-boiling material which could not be isolated in a pure state. The epoxide is reduced by lithium aluminium hydride in ether to 2 : 2 : 4-trimethylhexan-3-ol (3 : 5-dinitrobenzoate, m. p. and mixed m. p. 88—90°).

The epoxide (1 g.), shaken for 16 hr. with 0·5% sulphuric acid (5 c.c.), gave the glycol (0·4 g.), b. p. 108—110°/23 mm., with low-boiling material. Oxidative fission of the glycol with aqueous-alcoholic periodic acid gave ethyl methyl ketone and trimethylacetaldehyde.

Rearrangement of the epoxide by 30—50% aqueous sulphuric acid containing 2 : 4-dinitrophenylhydrazine gave two products both in poor yield: (*a*) orange needles (m. p. 146—146·5° (Found: C, 56·4; H, 6·8; N, 17·1. $C_{18}H_{22}O_4N_4$ requires C, 55·9; H, 6·9; N, 17·4%); and (*b*) bright yellow needles, m. p. 138°, in amount insufficient for analysis. The latter were also formed by using 90% phosphoric acid and a solution of the epoxide in light petroleum.

4-*Ethyl*-2 : 2-*dimethylhex*-3-*ene*.—This was obtained in 62% yield by heating the stearate of 4-ethyl-2 : 2-dimethylhexan-3-ol at 380° after the addition of some pyridines; it had b. p. 147°, n_D^{20} 1·4297, and gave only trimethylacetaldehyde and diethyl ketone on ozonolysis. 3 : 4-*Epoxy*-4-*ethyl*-2 : 2-*dimethylhexane*, b. p. 54—55°/12 mm., n_D^{20} 1·4243 (Found: C, 77·2; H, 12·7. $C_{10}H_{20}O$ requires C, 76·9; H, 12·9%), when heated to the b. p. with aqueous-alcoholic 50% sulphuric acid containing some 2 : 4-dinitrophenylhydrazine gave an oil from which a small amount of a yellow 2 : 4-dinitrophenylhydrazone separated in yellow needles, m. p. 131°, (from light petroleum), probably the dinitrophenylhydrazone of 2 : 2-diethyl-3 : 3-dimethylbutanal.

Hydration of the epoxide by 0·1N-sulphuric acid gave after 17 hr. only a poor yield of a glycol (0·18 g.), with volatile products. The glycol was oxidised by aqueous periodic acid, to diethyl ketone and trimethylacetaldehyde.

The authors are indebted to the Research Group of the Institute of Petroleum for grants and to the Department of Scientific and Industrial Research and to the Central Research Fund of the University of London for the purchase of special apparatus.

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383. *Hydrolysis of Amides and Related Compounds. Part I. Some Benzamides in Strong Aqueous Acid.*

By J. T. EDWARD and S. C. R. MEACOCK.

The rate of hydrolysis at 25° of the following amides reaches a maximum in approximately the acid strengths shown: benzamide, in 4·5M-hydrochloric acid or 3·5M-sulphuric acid; *p*-methoxybenzamide, in 3·0M-sulphuric acid; *p*-nitrobenzamide, in 4·5M-sulphuric acid. It is shown that these are the acid concentrations in which maximum rates are to be expected if account is taken of the ionization of the amides.

THE rates of the acid-catalysed hydrolysis of several amides go through a maximum as the concentration of acid is increased.[1-3] The concentrations for maximum rate depend on both the amide and the acid: for formamide, acetamide, and propionamide in sulphuric acid they are 4·75M, 2·5M, and 2·4M respectively.[2] These results may be explained in terms of the generally accepted mechanism for the hydrolysis of amides (I), in which the

[1] Euler and Ölander, *Z. phys. Chem.*, 1927, **131**, 107; Taylor, *J.*, 1930, 2741; Rabinovitch and Winkler, *Canad. J. Res.*, 1942, **20**, *B*, 73.
[2] Krieble and Holst, *J. Amer. Chem. Soc.*, 1938, **60**, 2976.
[3] Edward, Hutchison, and Meacock, *J.*, 1955, 2520.

rate-determining step is the attack of a water molecule on the conjugate acid (II) of the amide.[4] (The possibility that the *N*- rather than *O*-protonated form of the amide is the intermediate [5-7] is considered below.)

$$\underset{\text{(I)}}{R\cdot CO\cdot NH_2} \overset{H^+}{\rightleftharpoons} \underset{\text{(II)}}{R\cdot C(OH)=NH_2^+} \xrightarrow{H_2O} \text{Hydrolysis products}$$

Amides are strong enough bases to be appreciably protonated in 3—6M-mineral acid.[8] Below the concentration for maximum rate, the effect of increasing acid strength is chiefly to increase the concentration of the protonated intermediate; above the concentration for maximum rate, the effect is chiefly to decrease the concentration or activity of the water.[2]

The purpose of the present work was to see whether this hypothesis accounts quantitatively for the changes in rate of hydrolysis with acid concentration. We studied the hydrolysis of benzamide, *p*-methoxybenzamide, and *p*-nitrobenzamide, since it seemed probable that their ionization in acid could be determined by well-established spectrophotometric methods.[9, 10]

Experimental

Benzamide, *p*-methoxybenzamide, *p*-nitrobenzoic acid, and *p*-nitrobenzamide were recrystallized from water or aqueous ethanol to constant m. p. Aqueous acid solutions were made by dilution of reagent-grade acids with distilled water. They were standardized by titration against standard sodium hydroxide solution, except for concentrations of sulphuric acid above 80% which were determined by measurements of density.

Ionization Constants of p-*Methoxybenzamide and of Benzamide.*—The ultraviolet absorption of *p*-methoxybenzamide dissolved in water and in 17 different concentrations of aqueous sulphuric acid was measured in a 1 cm. quartz cell in a Beckman DU spectrophotometer. A selection of absorption curves is shown in Fig. 1. Absorption at 253 mμ is due mainly to the free amide (B) and at 280 mμ to its conjugate acid (BH^+). The difference ($\Delta\varepsilon = \varepsilon_{280} - \varepsilon_{253}$) between the extinction coefficients at these two wavelengths varied with acid concentration ($c_{H_2SO_4}$) as follows:

Temp. 18° ± 3°.

$c_{H_2SO_4}$ (% w/w) ...	0·00	0·56	2·41	4·51	9·31	13·9
Δε	−12,200	−12,100	−11,400	−11,500	−9520	−8580
$c_{H_2SO_4}$ (% w/w) ...	20·7	25·0	28·9	33·0	37·5	41·4
Δε	−6340	−3910	−1370	+1410	3420	6630
$c_{H_2SO_4}$ (% w/w) ...	44·3	48·5	51·1	53·1	56·0	97·0
Δε	8240	8500	9200	10,600	11,000	9800

In Fig. 3 Δε is plotted against the acidity function H_0 following the method used by Davis and Geissman [10] for determining pK values. The values of the acidity function for different concentrations of acid were found by reference to a large scale plot of Hammett and Deyrup's results.[11, 12] It is evident that in the complete conversion of the amide into its protonated form, Δε changes by approximately +23,100. Hence, any purely solvent effect of the changing acid concentration on absorption [9] being ignored, the extent of ionization at any acidity should be measured by:

$$[BH^+]/([B] + [BH^+]) = \Delta\varepsilon/23{,}100$$

Since

$$[B]/[BH^+] = K/h_0$$

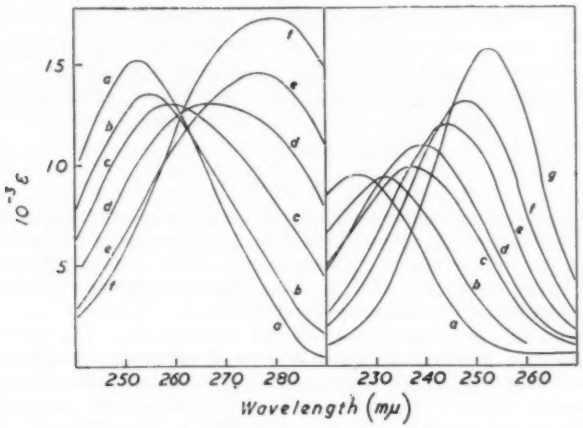
[4] Hantzsch, *Ber.*, 1931, **64**, 661; Taylor and Baker, "Sidgwick's Organic Chemistry of Nitrogen," Clarendon Press, Oxford, 1945, p. 144; Pauling, "The Nature of the Chemical Bond," Cornell University, Press, Ithaca, 1948, p. 208.
[5] Hammett, "Physical Organic Chemistry," McGraw Hill, New York, 1940, p. 365.
[6] Ingold, "Structure and Mechanism in Organic Chemistry," G. Bell and Sons, London, 1953, p. 786.
[7] Meloche and Laidler, *J. Amer. Chem. Soc.*, 1951, **73**, 1712.
[8] Hall, *J. Amer. Chem. Soc.*, 1930, **52**, 5115, and references cited there.
[9] Flexser, Hammett, and Dingwall, *ibid.*, 1935, **57**, 2103.
[10] Davis and Geissman, *ibid.*, 1954, **76**, 3507.
[11] Hammett and Deyrup, *ibid.*, 1932, **54**, 2721.
[12] Hammett and Paul, *ibid.*, 1934, **56**, 827.

where K is the ionization constant for the equilibrium $BH^+ \rightleftharpoons B + H^+$, and h_0 (= −antilog H_0) is Hammett's non-logarithmic acidity function,[13] the equation may be written:

$$h_0/(K + h_0) = \Delta\varepsilon/23{,}100$$

The theoretical curve corresponding to this equation, with $K = 40$ ($pK = -1{\cdot}60$) is shown in Fig. 3, and is in reasonable agreement with the experimental values. The systematic deviations from the curve are probably to be attributed to solvent effects.[9, 11]

FIGS. 1 & 2. *Absorption spectra of* p-*methoxybenzamide* (Fig. 1) *and of benzamide* (Fig. 2) *in sulphuric acid.*



	Curve	*a*	*b*	*c*	*d*	*e*	*f*	*g*
Fig. 1	Acid, %	0·0	13·9	25·0	33·0	41·4	97·0	—
Fig. 2	,,	0·0	27·3	38·3	41·4	58·1	73·2	97·0

In the same way the absorption of benzamide dissolved in water and in 20 different concentrations of sulphuric acid was determined. A selection of curves is given in Fig. 2. Absorption at 225 mμ is evidently due mainly to the free amide, and at 240 mμ to its conjugate acid. The difference ($\Delta\varepsilon = \varepsilon_{240} - \varepsilon_{225}$) between the extinction coefficients at these two wavelengths varied with acid concentration as follows:

Temp. 18° ± 3°.

$c_{H_2SO_4}$ (% w/w) ...	0·00	0·56	2·19	4·51	9·31	13·9	21·7	27·3
	−3920	−4050	−3920	−3860	−3340	−2920	−1830	−420
$c_{H_2SO_4}$ (% w/w)	33·0	38·3	41·4	47·3	53·1	55·3	58·1	59·9
	+1500	3130	4100	5510	6790	6950	6940	6970
$c_{H_2SO_4}$ (% w/w) ...	62·3	66·2	73·2	86·2	97·0			
	7900	7610	7550	8230	7290			

These results fit best the theoretical curve for $K = 71$ ($pK = -1{\cdot}85$) (Fig. 3). The increase in ε and the shift of $\lambda_{max.}$ to longer wavelengths in acid concentrations above 62·3% (Fig. 2) are then to be ascribed wholly to the solvent effect of the sulphuric acid, which is known to be greatest in the range 60—85% acid.[11] Shifts of similar or greater magnitude have been noted with other compounds.[10, 14]

The analysis of the spectral results by the original procedures of Flexser *et al.*[9] rather than that of Davis and Geissman led to substantially the same pK values.

The ionization constant of *p*-nitrobenzamide could not be determined by spectroscopic methods because the change in absorption on ionization was too small: in water, $\lambda_{max.}$ 265 mμ, log $\varepsilon_{max.}$ 4·06; in 47·3% sulphuric acid, $\lambda_{max.}$ 265·5 mμ, log $\varepsilon_{max.}$ 4·09; in 97% sulphuric acid, $\lambda_{max.}$ 266·5 mμ, log $\varepsilon_{max.}$ 4·18.

[13] Ref. 5, p. 271.
[14] Brand, *J.*, 1950, 997.

Rate Measurements for the Hydrolysis of Benzamide and p-*Methoxybenzamide.*—These were carried out according to the procedure described previously,[3] the reaction being followed by "formol" titration [15] of the ammonium ion formed. In the excess of acid used the hydrolyses were of the first order with respect to the amide, as shown by the linearity of plots of log $[NH_4^+]$ against time. The apparent first-order constants (k_e), found by multiplying the slope of these curves by 2·303, are shown in Fig. 4. The constants for benzamide in 1N- ($6{\cdot}8 \times 10^{-4}$ hr.$^{-1}$)

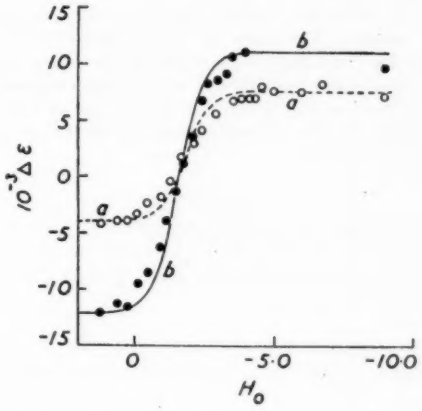
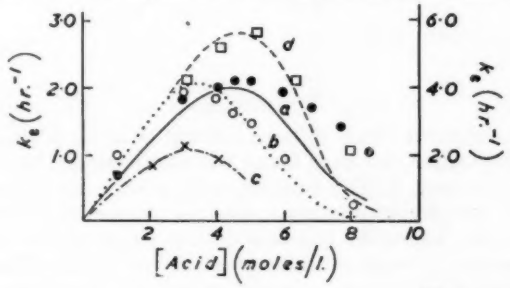


FIG. 3. *Variation of* $\Delta\varepsilon$ *for benzamide* (*a*) *and* p-*methoxybenzamide* (*b*) *with acidity function* (H_0) *of aqueous sulphuric acid.*

FIG. 4. *Variation in first-order constants with acid concentration.*



		Theor.	Exper.
Left-hand scale	Benzamide in HCl	*a*	●
	Benzamide in H_2SO_4	*b*	○
	p-Methoxybenzamide in H_2SO_4	*c*	×
Right-hand scale	*p*-Nitrobenzamide in H_2SO_4	*d*	□

and 4N-hydrochloric acid ($2{\cdot}00 \times 10^{-3}$ hr.$^{-1}$) proved to be in good agreement with values ($6{\cdot}9 \times 10^{-4}$ and $2{\cdot}00 \times 10^{-3}$ hr.$^{-1}$, respectively) calculated for this temperature by interpolation of Arrhenius plots of Rabinovitch and Winkler's results; [1] these investigators used a different method for estimating the ammonia formed.

Rate Measurements for the Hydrolysis of p-*Nitrobenzamide.*—The solubility of *p*-nitrobenzamide was too small in sulphuric or hydrochloric acid weaker than about 6M for the formol titration to be used. However, the reaction could be followed spectrophotometrically since the absorption spectra of *p*-nitrobenzamide and of *p*-nitrobenzoic acid are appreciably different in sodium carbonate solution (Fig. 5) although almost identical in aqueous acid. Aliquot parts (2 ml.) of a solution of *p*-nitrobenzamide (*ca.* 40 mg., accurately weighed) in aqueous sulphuric acid (100 ml.), kept at 25·00° ± 0·05° in a shaded bottle in a thermostat, were withdrawn at intervals and diluted to 100 ml. with 0·202N-sodium carbonate (for runs in 3·08M-sulphuric acid)

[15] Northrop, *J. Gen. Physiol.*, 1926, **9**, 767.

or 0·298N-sodium carbonate (for runs in 4·15M-, 5·22M-, and 6·24M-sulphuric acid). The absorption was measured in the region 245—300 mμ inclusive. Hydrolysis could be followed only to about 40% completion, after which *p*-nitrobenzoic acid began to crystallize from the solution.

In a modification of this method the sodium carbonate solution was extracted with an equal volume of ethyl acetate before the spectroscopic examination; this had been shown to remove 91·5 ± 0·1% of the *p*-nitrobenzamide but none of the *p*-nitrobenzoate ion. The partition coefficient for *p*-nitrobenzamide was shown to be independent of concentration in the ranges studied. The effect of the extraction was to increase the total change in optical density during a run; readings were made in the range 285—300 mμ, in which ethyl acetate is transparent. The results agreed well with those obtained by the first method. The first-order constants shown on Fig. 4 are the average of at least three values found by following the reaction at different wave-lengths according to the first method, and three by the second method.

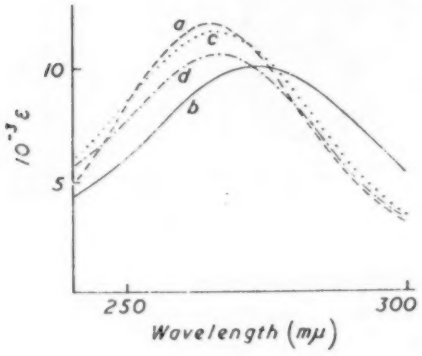


FIG. 5. *Absorption spectra of* p-*nitrobenzoic acid in* 2M-*sulphuric acid* (*a*) *and in* 0·089N-*sodium carbonate* (*b*); *of* p-*nitrobenzamide in water* (*c*) *and in* 0·089N-*sodium carbonate* (*d*).

DISCUSSION

While ionization frequently leads to large spectral changes, it does not invariably do so.[9] In the present instance, we have found the ultraviolet absorption of *p*-nitrobenzamide to be almost the same in 97% sulphuric acid as in water, although in the former solvent it should be completely protonated, like the weaker base *p*-nitrobenzoic acid.[16] However, although the ionization constant of the amide cannot be determined by absorption measurements, a rough estimate of it may be obtained from the application of Hammett's equation,[17] $pK_0 - pK = \rho\sigma$, pK_0 in this case being the ionization constant of benzamide, pK the ionization constant of a *para*- or *meta*-substituted benzamide, ρ a constant characteristic of the ionization of benzamides, and σ a constant characteristic of the *meta*- or *para*-substituent. When Hammett's σ values of −0·268 for the *p*-methoxy- and +0·778 for the *p*-nitro-group are used, it follows that σ is +0·933, and hence for *p*-nitrobenzamide the pK is −2·58 and K is 380.

The amides and their conjugate acids are involved in the equilibria:

$$B + H_3O^+ \underset{}{\overset{K_1}{\rightleftharpoons}} BH^+ + H_2O \overset{K_2}{\rightleftharpoons} M^+ \xrightarrow{k} \text{Hydrolysis products}$$

where K_1 and K_2 are equilibrium constants, M^+ is the transition complex for the hydrolysis, and k is a velocity constant. The Brønsted [18] equation for the rate v of the hydrolysis is:

$$v = k[M^+] = kK_2[B][H_3O^+]f_B f_{H_3O^+}/(f_{M^+}K_1) \quad . \quad . \quad . \quad . \quad (1)$$

the quantities in brackets being concentrations and the f's activity coefficients. The

[16] Hantzsch, *Z. phys. Chem.*, 1908, **61**, 257; **65**, 41.
[17] Ref. 5, p. 186.
[18] Brønsted, *Z. phys. Chem.*, 1922, **102**, 169; ref. 6, p. 48.

term $(f_B f_{H_3O^+}/f_{M^+})$ is approximately constant,[19] and may be merged with the other constants into a second-order rate constant k_2, giving :

$$v = k_2[B][H_3O^+]$$

However, the experimental first-order constants k_e, giving the rate of the reaction in different concentrations of excess acid, are based on the change in stoicheiometric concentration of amide, ionized and un-ionized :

$$v = k_e([B] + [BH^+])$$
$$= k_e[B](K + h_0)/K$$

Hence
$$k_e = k_2K[H_3O^+]/(K + h_0) \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (2)$$

For very weak bases such as esters, $K \gg h_0$ in the range of acid concentrations being considered here, and so equation (2) simplifies to :

$$k_e = k_2[H_3O^+]$$

This gives the linear dependence of experimental first-order constants on the concentration of oxonium ion [19] which has been found for the hydrolysis of esters,[20] lactones,[21] and alkyl phosphates.[22] However, when $K \ll h_0$, equation (2) simplifies to :

$$k_e = k_2K[H_3O^+]/h_0$$

Since h_0 increases with concentration much more rapidly than $[H_3O^+]$ when mineral acid concentrations exceed about 2M,[11, 12] k_e will decrease in high acid concentrations. {When

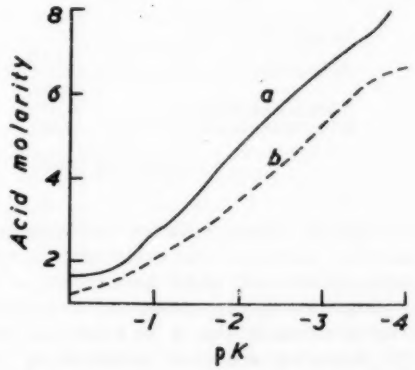


FIG. 6. *Effect of basicity of substrate on the concentration of hydrochloric (a) or sulphuric acid (b) in which the first-order rate constant of hydrolysis is maximal.*

$K \ll h_0$, ionization to BH^+ is substantially complete; the decrease in rate of hydrolysis can be regarded as due to the decreasing availability of water, since $[H_2O] = K_w[H_3O^+]/h_0$, where K_w is the equilibrium constant for the reaction $H_3O^+ \rightleftharpoons H_2O + H^+$.} At a certain acid concentration, which depends on the ionization constant K of the substrate, and on the variation with concentration of $[H_3O^+]$ and of h_0 for the acid concerned, k_e will reach a maximum. The variation of these concentrations for maximal rate with the pK ($= -\log K$) of the substrate, in either hydrochloric or sulphuric acid, is shown in Fig. 6. In calculating these curves, the concentration of oxonium ion in aqueous hydrochloric acid has been assumed to be identical with the stoicheiometric acid concentration in the range studied; [23] the concentration in aqueous sulphuric acid has been estimated from Young's results [24] from Raman spectral studies. The acidity functions for different

[19] Ref. 5, p. 276.
[20] Bell, Dowding, and Noble, *J.*, 1955, 3106.
[21] Long, McDevit, and Dunkle, *J. Phys. Colloid Chem.*, 1951, **55**, 829.
[22] Barnard, Bunton, Llewellyn, Oldham, Silver, and Vernon, *Chem. and Ind.*, 1955, 760.
[23] Robinson and Stokes, "Electrolyte Solutions," Butterworths, London, 1955, pp. 362, 370 *et seq.*
[24] Young, *Rec. Chem. Progr.*, 1951, **12**, 81; Dr. V. Gold, personal communication.

concentrations of hydrochloric [12, 20, 25] and sulphuric acid [11, 12] have been determined from large-scale plots of data in the literature.

In the Table the pK's of various amides, as predicted (according to Fig. 6) from the acid concentrations for maximal rates, are compared with experimental values. The agreement is reasonably good. In the latest study of the ionization of acetamide,[26] two ionization constants, $pK_1 = +0{\cdot}37$ and $pK_2 = -1{\cdot}40$, have been reported. The latter value is in good agreement with the predicted value. It is possible that the first ionization constant refers to the formation of a cation (B_2H^+) made up of two molecules of amide and one proton. Stable salts of such cations are well known.[27] However, it is unlikely that such a cation is an important intermediate in the hydrolysis of acetamide, since it would necessitate the reaction rate's being of second order with respect to acetamide. The reaction appears to be of first order even in dilute acid solution,[1-3] in which the formation of B_2H^+ relative to BH^+ should be favoured.

Relation between pK*'s of amides and the acid concentrations* (c_M, *in moles/l.*) *in which rates of hydrolysis are maximal at* 25°.

Amide	Acid	c_M	pK Predicted	pK Found
Formamide [a]	HCl	6	−2·60	—
	H_2SO_4	4·75	−2·75	
Acetamide [a]	HCl	3·25	−1·33	−0·5; [6] −0·04 [a] −1·40 [26]
	H_2SO_4	2·5	−1·35	
Propionamide [a]	HCl	3·20	−1·30	
	H_2SO_4	2·40	−1·30	
Benzamide	HCl	4·5	−1·90	−1·85 (18° ± 3°)
	H_2SO_4	3·5	−2·01	
p-Methoxybenzamide	H_2SO_4	3·0	−1·70	−1·60 (18° ± 3°)
p-Nitrobenzamide	H_2SO_4	4·5	−2·60	−2·58 (18° ± 3°)

[a] Lemaire and Lucas, *J. Amer. Chem. Soc.*, 1951, **73**, 5198.

The pK values predicted for formamide and propionamide seem plausible, since they have the same qualitative relation to the pK of acetamide that the pK's [28] of formic (3·75) and propionic acid (4·87) have to that of acetic acid (4·76) in water at 25°.

Equation (2) also covers the variation in rate with acid concentration reasonably well. This is shown in Fig. 4, in which the theoretical curves have been calculated by using the following arbitrary values of k_2: benzamide, $6{\cdot}4 \times 10^{-2}$; *p*-methoxybenzamide, $3{\cdot}8 \times 10^{-2}$; *p*-nitrobenzamide, $11{\cdot}5 \times 10^{-2}$ hr.$^{-1}$ mole^{-1}; and assuming the pK values of the base to be the same at 25° as at 18° ± 3°. Agreement is reasonably satisfactory at lower acid concentrations, but at higher concentrations the experimental values tend to be higher than predicted. However, deviations in this direction have been noted in the hydrolysis of esters [20] and in many other acid-catalysed reactions.[29] They may perhaps be attributed to a systematic variation in the term $(f_B f_{H_3O^+}/f_{M^+})$ as the concentration of acid is increased.[30]

$R{\cdot}CO{\cdot}NH_2^+$ (III)

While the foregoing argument shows that the rates of hydrolysis in acid of different strengths may be explained by assuming as intermediate the *O*-protonated

[25] Braude, *J.*, 1948, 1971; Paul, *J. Amer. Chem. Soc.*, 1954, **76**, 3236.
[26] Goldfarb, Mele, and Gutstein, *ibid.*, 1955, **77**, 6194.
[27] Werner, *Ber.*, 1903, **38**, 154; Walden, *Bull. Acad. St. Pétersbourg*, 1911, 1055; *Chem. Zentr.*, 1912, **16**, I, 122; White, *J. Amer. Chem. Soc.*, 1955, **77**, 6215.
[28] Ref. 23, p. 496.
[29] Long and Purchase, *J. Amer. Chem. Soc.*, 1950, **72**, 3267; Paul, *ibid.*, 1952, **74**, 141; McIntyre and Long, *ibid.*, 1954, **56**, 3240; Bell and Brown, *J.*, 1954, 774; Gold and Hilton, *J.*, 1955, 843; Gold and Satchell, *J.*, 1955, 3622.
[30] Long and McIntyre, *J. Amer. Chem. Soc.*, 1954, **76**, 3243.

form (BH^+; II) it does not exclude the *N*-protonated form ($B'H^+$; III). The latter will be a very much less powerful base,[4] *i.e.* $K_1' \gg K_1$ for the equilibria :

$$BH^+ + H_2O \underset{}{\overset{K_1}{\rightleftharpoons}} B + H_3O^+ \overset{K_1'}{\rightleftharpoons} B'H^+ + H_2O \overset{K_2'}{\rightleftharpoons} M^+ \longrightarrow \text{Products}$$

However, it will be correspondingly more reactive (*i.e.*, $K_2' \gg K_2$). It is obvious that the postulation of this mechanism leads to an equation differing from (1) only in having K_1' and K_2' in place of K_1 and K_2. The two mechanisms are accordingly kinetically indistinguishable.[31]

We are grateful to the Medical Research Council of Ireland for a research grant (to S. C. R. M.), to Dr. V. Gold for information, and to Professor W. Cocker for constant support and encouragement.

CHEMICAL LABORATORY, TRINITY COLLEGE, DUBLIN. [*Received, August 10th*, 1956.]

[31] Frost and Pearson, " Kinetics and Mechanism," Wiley, New York, 1953, p. 264.

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384. *Hydrolysis of Amides and Related Compounds. Part II.* Acetylglycine, Piperazine-2 : 5-dione, and Gelatin in Concentrated Hydrochloric Acid.*

By J. T. EDWARD and S. C. R. MEACOCK.

At 61° the rate of hydrolysis of acetylglycine is maximal in about 5M-hydrochloric acid. No maximum was found in the rate of hydrolysis of piperazine-2 : 5-dione or of gelatin as the concentration of hydrochloric acid was increased to 10M.

MANY studies have been made of the kinetics of the hydrolysis of peptides and proteins in aqueous acids,[1] but there appear to have been no attempts to discover whether the rates pass through a maximum as the concentration of acid is increased (cf. Part I). We have accordingly studied the hydrolysis at 61° of acetylglycine, piperazine-2 : 5-dione, and gelatin in hydrochloric acid of varying concentrations, using the " formol " titration [2] to estimate the amino-groups liberated during the hydrolysis.

The rate of hydrolysis of acetylglycine (see Table) was maximal in about 5N-acid at this temperature. This is likely [3] to be the concentration for maximal rate at 25° also, and hence indicates a pK_a of the peptide linkage of about -2.[4] This agrees with a recent spectrophotometric result (pK_a $-1{\cdot}92$)[5] and is about the value to be expected from a pK_a of $-1{\cdot}4$ for acetamide when the inductive effect of the $\cdot CH_2 \cdot CO_2H$ group [6] is considered.

The rate of hydrolysis of piperazine-2 : 5-dione was a roughly linear function of acid concentration up to the highest concentration investigated (10·18N). This rate refers to its hydrolysis to glycylglycine; the hydrolysis of the latter to glycine goes fifty times more slowly in 2N-hydrochloric acid [7] and (as is shown below) probably in the other concentrations employed, and hence can be ignored. The absence of a maximum rate in this range of acid concentrations indicates a pK_a of the peptide linkage below -4.[4]

As expected,[1] the hydrolysis of gelatin, involving many different types of peptide linkages, did not obey first-order kinetics. Accordingly the quarter-life was chosen as a

* Part I, preceding paper.

[1] Leach, *Rev. Pure Appl. Chem.*, 1953, **3**, 25, and references therein.
[2] Northrop, *J. Gen. Physiol*, 1926, **9**, 767.
[3] Edward, Hutchison, and Meacock, *J.*, 1955, 2520.
[4] Edward and Meacock, preceding paper.
[5] Goldfarb, Mele, and Gutstein, *J. Amer. Chem. Soc.*, 1955, **77**, 6194.
[6] Cohn and Edsall, " Proteins, Amino Acids and Peptides," Reinhold, New York, 1943, p. 116 *et seq.*
[7] Hammel and Glasstone, *J. Amer. Chem. Soc.*, 1954, **76**, 3741.

XUM

Rates of hydrolysis in hydrochloric acid at 61°.

k_a = first-order velocity constant in min.$^{-1}$. $t_{1/4}$ = time for 25% hydrolysis in hr. Acid concentrations are in moles/l.

Acetylglycine

[HCl]	1·00	2·00	3·00	4·00	5·00	6·00	8·21
10^3k_a	0·86	1·62	2·26	2·51	{2·69, 2·67}	2·35	1·34

Piperazine-2 : 5-dione

[HCl]	1·00	2·00	3·00	4·00	5·00	7·52	8·36	10·18
10^3k_a	0·82	1·95	2·67	3·09	4·00	5·18	5·12	6·24
10^3k_a/[HCl]	8·2	9·7	8·9	7·7	8·0	6·9	6·1	6·1

Gelatin

[HCl]	3·00	4·94	5·25	7·00	10·4
$t_{1/4}$	5·1	2·9	2·6	2·5	1·6
[HCl] × $t_{1/4}$/10	1·5	1·4	1·4	1·7	1·7

convenient measure of the stabilities in the different acid concentrations;[8] its reciprocal will be proportional to the relative rate of hydrolysis. For this material also, the rate is roughly proportional to the acid concentration up to 10·4N, so that the average pK_a of the peptide linkages must be below −4.[4] A pK_a value of about −4 has been reported from spectrophotometric studies.[9] With both gelatin and piperazine-2 : 5-dione it is evident that the neighbouring peptide linkages strongly depress each other's basicity. Base-weakening effects of proximal peptide linkages on other groups have been observed in many simple compounds.[6]

The differing basicities of amides enable one to choose conditions for obtaining some degree of specificity in their hydrolysis. Thus acetamide[3] is hydrolysed about 50% more rapidly than piperazine-2 : 5-dione in 1N-hydrochloric acid, but about ten times more slowly in 8N-acid. However, there is likely to be no important change in the relative stabilities of the different peptide linkages of proteins (apart from those involving serine and threonine[10]) over the range 1N—10N-hydrochloric acid. The pK_a's of the peptide linkages of proteins are about −4; in the smaller peptides they will be less basic because of the proximity of the charged amino-group.[6] Consequently, in the range of acidities being considered (up to H_0 of −3·6) the rates of hydrolysis should be proportional to the concentration of hydroxonium ion,[4] and hence the order of stabilities should be the same in different strengths of acid. This is in agreement with the limited evidence at present available.[11]

Experimental

Acetylglycine (m. p. 207—208°) and piperazine-2 : 5-dione (m. p. 309—310°) were purified by recrystallization from water to the m. p.s indicated. Nelson No. 3 gelatin was used without further treatment. Its amine titre (0·400 g. of gelatin ≡ 30·8 c.c. of 0·1N-sodium hydroxide in the " formol " titration) was constant after 24 hours' hydrolysis in 7N-hydrochloric acid at 100°, and was taken to represent 100% hydrolysis. Rate measurements were carried out as described previously[3] on 0·3—0·4M-solutions of acetylglycine or piperazine-2 : 5-dione or 4% solutions of gelatin in acid. Results for two typical runs are shown below :

Acetylglycine. 0·339M; *with* 5·00N-*hydrochloric acid*

Time (min.)	31	54	140	177	220	271	340
Hydrolysis (%)	9·2	13·9	32·2	38·1	44·9	51·8	56·7

$k = 2·67 \times 10^{-3}$ min.$^{-1}$.

Piperazine-2 : 5-dione. 0·339M; *with* 2·00N-*hydrochloric acid.*

Time (min.)	8	22	30	40	53	74	91
Hydrolysis (%)	20·5	39·5	49·5	57·1	67·0	76·4	78·5

$k = 1·95 \times 10^{-2}$ min.$^{-1}$.

Chemical Laboratory, Trinity College, Dublin. [*Received, September 17th*, 1956.]

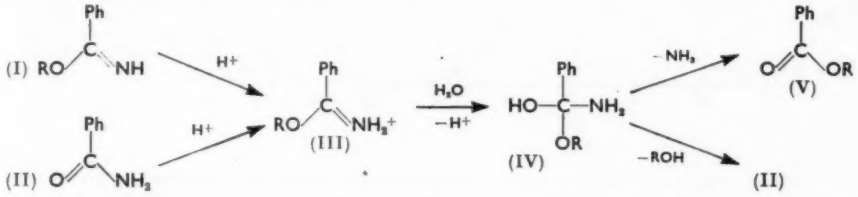
[8] Cf. Sanger, *Adv. Protein Chem.*, 1952, **7**, 1.
[9] Goldfarb and Gutstein, Abs. Papers 126th Meeting Amer. Chem. Soc., 1954, 61c.
[10] Elliott, *Biochem. J.*, 1952, **50**, 542.
[11] Martin, *Nature*, 1955, **175**, 771; Hirohata, Kanda, Nakamura, Izumiya, Nagamatsu, Ono, Fujii, and Kimitsuki, *Z. physiol. Chem.*, 1953, **295**, 368; Harris, Cole, and Pon, *Biochem. J.*, 1956, **62**, 154.

385. *Hydrolysis of Amides and Related Compounds. Part III.* Methyl Benzimidate in Aqueous Acids.*

By J. T. Edward and S. C. R. Meacock.

The rate of hydrolysis of methyl benzimidate in aqueous hydrochloric and sulphuric acid decreases sharply with acid concentration after protonation of the base is nearly complete. It is concluded that this hydrolysis may proceed by a mechanism similar to that for the hydrolysis of benzamide.

The hydrolysis of methyl benzimidate (I; R = Me) in aqueous acids affords chiefly methyl benzoate (V; R = Me) and ammonium ion, but in water small amounts of benzamide (II) and methanol are also formed.[1,2] The kinetics of the reaction were studied extensively by Stieglitz and his co-workers,[1] who showed that with a deficiency of hydrochloric acid the rate was proportional to the concentration of the protonated from (III; R = Me). Since methyl benzimidate is a moderately strong base (pK_a' 5·67),[1] its protonation approaches completion in solutions more acid than about pH 3, and it would be expected that the rate would become constant with increasing acidity. However, in >0·1N-hydrochloric acid the rate began to drop (see Fig. 1).



It has been shown [3] that the kinetics of the hydrolysis of benzamide (II) are consistent with a mechanism involving the very similar ion (III; R = H). If the rate-determining step in both hydrolyses is the attack of a water molecule on such an ion (III; R = H or Me) to give the labile intermediate (IV; R = H or Me), it may be predicted that (*a*) the rates of hydrolysis of both compounds should be of the same order when based on the concentration of the ionized species (III; R = H or Me), and (*b*) the decrease in the rate of hydrolysis of methyl benzimidate with increasing concentration of acid should be described by the equation found valid for benzamide.[3] The present paper describes work to test these predictions.

Experimental

Materials.—Methyl benzimidate hydrochloride [4] had m. p. 105—106° (decomp.) after recrystallization from glacial acetic acid–dry ether. On hydrolysis in N-hydrochloric acid at 100° for 4 hr. it afforded 100·1% of the calculated amount of ammonium ion, as estimated by "formol" titration.[5] *Methyl benzimidate hydrogen sulphate*, prepared by adding the calculated quantity of 96% sulphuric acid to methyl benzimidate in dry ether, after three crystallizations as above, melted at 120—121° [Found: C, 41·7; H, 4·7; SO_4 (as $BaSO_4$), 32·8. $C_8H_{11}O_6NS$ requires C, 41·2; H, 4·7; SO_4, 33·1%]. The imidate salts were kept in a vacuum-desiccator.

Analytical Methods.—The apparent dissociation constant pK_a' of methyl benzimidate hydrochloride was found by potentiometric titration of a 0·14M-solution with 0·1N-sodium hydroxide (glass electrode) to be 5·8. Stieglitz *et al.*[1] reported pK_a' 5·68. On hydrolysis it

* Part II, preceding paper.

[1] Stieglitz, *Amer. Chem. J.*, 1908, **39**, 29, 166; Derby, *ibid.*, p. 437; McCracken, *ibid.*, p. 586; Schlesinger, *ibid.*, p. 719.

[2] Mengelberg, *Chem. Ber.*, 1954, **87**, 1425.

[3] Edward and Meacock, *J.*, 1957, 2004.

[4] Pinner, *Ber.*, 1883, **16**, 352.

[5] Northrop, *J. Gen. Physiol.*, 1926, **9**, 767.

forms ammonium ion (pK_a' 9·2) and methyl benzoate, and possibly a trace of benzamide and methanol; the further hydrolysis of benzamide [3] and methyl benzoate [6] to benzoic acid will be negligible under the conditions of these experiments. Consequently, in the titration of the reaction solution from pH 3·7 to pH 8·0 (glass electrode) (method *a*), 98·5% of the conjugate acid of methyl benzimidate and 5·9% of the ammonium ion will be neutralized. Similarly, the formol titration according to Northrop [5] (method *b*) will in the present instance measure ammonium ion and also the 4·7% of the conjugate acid of methyl benzimidate still unneutralized at pH 7·0. However, while these two methods do not indicate the stoicheiometric concentration either of protonated methyl benzimidate or of ammonium ion, the change in the measurements during the reaction will be proportional to the extent of the reaction, it being assumed that the reaction is of first order with respect to methyl benzimidate in excess of aqueous acid. Reaction rates found by each method were in fair agreement with each other and with the results of Derby,[1] who used a different method (Fig. 1).

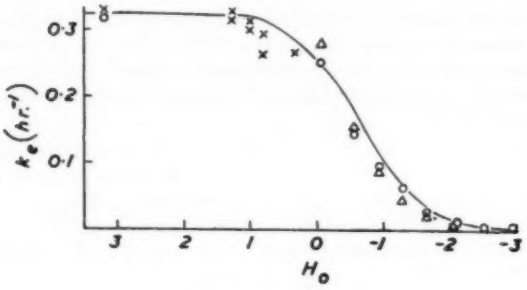


FIG. 1. *Hydrolysis of methyl benzimidate in hydrochloric acid of varying strengths (expressed as the acidity function H_0).*

Sources of experimental points: × *Derby.*[1] △ *Present work: reaction followed by method (a).* ○ *Present work: reaction followed by method (b).*

Rate Measurements.—A known weight of methyl benzimidate salt, sufficient to give a 0·1—0·2M-solution, was added with shaking at zero time to the acid solution (100·0 ml.), kept at 25·00° ± 0·05°. The salt dissolved in less than 1 min. At intervals aliquot parts (10·0 ml.) were pipetted into a mixture of ice and sufficient 2N-sodium hydroxide to bring the pH to about 3. This solution was then titrated in less than 5 min. Method *a* was used for following hydrolyses of the hydrochloride in 1·00, 2·00, 3·00, 4·00, 5·00, and 6·00M-hydrochloric acid,

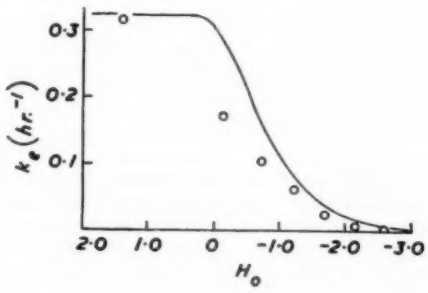


FIG. 2. *Hydrolysis of methyl benzimidate in sulphuric acid of varying strengths.*

Guggenheim's method [7] being used for evaluating rate constants. Method *b* was used for following hydrolyses of the hydrochloride in distilled water (pH of solution 3·2) and in 1·00, 2·00, 3·00, 4·00, 5·00, 6·15, 7·38, and 8·20M-hydrochloric acid; and of the acid sulphate in distilled water (pH of solution 1·4) and in 1·00, 2·00, 3·00, 4·00, 5·00, and 6·00M-sulphuric acid, rate constants being evaluated by the usual graphical method. The results are given in Figs. 1 and 2, the empirical first-order rate constants being plotted against acidity function (H_0) instead of acid concentration.

[6] Chmiel and Long, *J. Amer. Chem. Soc.*, 1956, **78**, 3326.
[7] Guggenheim, *Phil. Mag.*, 1926, **2**, 538.

Discussion

If the hydrolysis of methyl benzimidate has as its rate-determining step the reaction of a molecule of water with the ion (III; R = Me) it would be expected [3] that the empirical first-order rate constant k_e would vary with acid concentration according to the equation

$$k_e = k_2K_1[H_3O^+]/(K_1 + h_0)$$

k_2 being a second-order rate constant for the reaction (III; R = Me) + $H_2O \longrightarrow$ (IV), K_1 the equilibrium constant for the reaction (III; R = Me) + $H_2O \rightleftharpoons$ (I; R = Me) + H_3O^+, and h_0 the non-logarithmic acidity function.[8] Since for methyl benzimidate $h_0 \gg K_1$ for the acid concentrations used in our experiments, the equation may be simplified to:

$$k_e = k_3[H_3O^+]/h_0 \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (1)$$

This equation gives expression to the fact that the decrease in the rate of hydrolysis with increase of acid concentration is governed by the decreasing concentration of water after complete protonation of the substrate. (The water concentration for kinetic purposes is

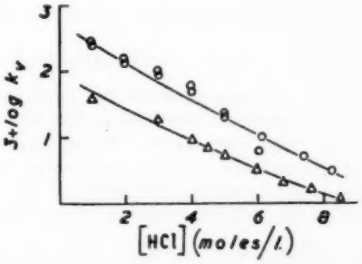


Fig. 3. *Hydrolysis of methyl benzimidate* (○) *and of benzamide* (△) *in hydrochloric acid.*

proportional to $[H_3O^+]/h_0$,[3] and *not* to the stoicheiometric water concentration, presumably because of the various effects of the ions in binding water, etc.) The theoretical curves shown in Figs. 1 and 2 have been calculated from this equation, h_0 and the oxonium-ion concentrations for the different acid concentrations being obtained as previously,[3] and k_3 being assigned the value of 0·325 hr.$^{-1}$. The experimental values for hydrolyses in hydrochloric acid (Fig. 1) are in reasonable agreement with the theoretical curve, but in sulphuric acid (Fig. 2) the agreement is less satisfactory.

Although in M-hydrochloric acid the hydrolysis of methyl benzimidate is about 400 times faster than that of benzamide, the difference is due chiefly to the almost complete protonation of the benzimidate as compared with only 1·6% protonation of the benzamide. Account may be taken of this difference by defining a first-order rate constant k_ψ based on the concentration of the protonated forms (III; R = H or Me) only. This is related to the empirical first-order constant k_e (which is based on the stoicheiometric concentration of amide or imidate) by the equation

$$k_\psi = k_e([B] + [BH^+])/[BH^+] = k_e(K'_a + h_0)/h_0$$

where *B* is (I; R = Me) or (II), BH^+ is (III; R = H or Me), and K'_a is the equilibrium constant of the reaction, $BH^+ \rightleftharpoons B + H^+$. It is found (Fig. 3) that in M-hydrochloric acid the value of k_ψ for methyl benzimidate is only about five times greater than that for benzamide, while in 8M-acid it is only about 2·5 times greater. It would be difficult to predict *a priori* which of the ions (III; R = H) and (III; R = Me) would react more readily with water, but obviously it would be expected that the difference would be small. The present results, while not proving the orthoamide derivative (III; R = H) to be an

[8] Hammett, "Physical Organic Chemistry," McGraw-Hill, New York, 1940, p. 271.

intermediate in the hydrolysis of benzamide, show that it would have about the required reactivity.

Some doubt about this mechanism is raised by the failure to observe during hydrolysis any exchange of the oxygen of benzamide with that of water.[9] The intermediate (IV; R = H) might be expected to regenerate some benzamide by the elimination of water, by analogy with the formation of benzamide from methyl benzimidate by the elimination of methanol.[1,2] However, the latter type of reaction has been observed only in solutions of low acidity, and it is possible that the intermediates (IV; R = H or Me) have an overwhelming tendency to eliminate ammonia in moderately acidic solutions. For the moment the precise mechanism of the hydrolysis of amides must be considered unsettled.

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[9] Bender and Ginger, *J. Amer. Chem. Soc.*, 1955, **77**, 348.

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386. *Researches on Acetylenic Compounds. Part LV.* The Preparation and Properties of some Polyacetylenic Acids and their Derivatives.*

By E. R. H. JONES, J. M. THOMPSON, and M. C. WHITING.

Conjugated di- and tri-acetylenic acids are prepared by carboxylation of the bromomagnesium derivatives of the corresponding monosubstituted di- and tri-acetylenic hydrocarbons. The preparation of some of the latter, and the chemical properties of the derived acids, are briefly discussed. Light absorption data are recorded; the ultraviolet absorption spectra of the nitriles resemble those of the simple polyacetylenes.

THE reaction between alkynylmagnesium bromides and carbon dioxide, preferably under pressure, affords a convenient route to αβ-acetylenic acids; its application to the analogous preparation of conjugated di- and tri-acetylenic acids has already been summarised.[1] Since then details have been published for the preparation of hexa-2 : 4-diynoic acid,[2] and syntheses of octa-2 : 4 : 6-triynoic[3] and dec-8-en-2 : 4 : 6-triynoic[4] acid by other routes have been described.

Like penta-1 : 3-diyne, hexa-1 : 3-diyne and nona-1 : 3-diyne readily give the corresponding acids on Grignard carboxylation. Using the bisbromomagnesium derivative, Dr. J. B. Armitage converted 2-methylhexa-3 : 5-diyn-2-ol into the corresponding hydroxy-acid. Attempts to apply the same method to the preparation of conjugated triacetylenic acids, however, depended upon the availability of the corresponding 1 : 3 : 5-triynes, and, whereas the monosubstituted derivatives of diacetylene[5] may, with appropriate precautions, be purified by distillation and manipulated at or near room temperature, the corresponding triacetylenes are much less stable. Although distillation of such compounds at *ca.* 20° has been reported,[6] further experience has shown that this is hazardous and often ineffective; thermal decomposition of 1 : 3 : 5-triynes occurs in the range −10° to 30°, even at 10^{-1} mm., and may be very violent. It was therefore necessary to devise a method of preparing such hydrocarbons which gave directly a product of high purity.

Cook *et al.*[6] prepared these triynes (*a*) by alkylation of monosodiotriacetylene, obtained by dehydrohalogenation of 1 : 6-dichlorohexa-2 : 4-diyne, and (*b*) by condensation of the

* Part LIV, *J.*, 1956, 4765.

[1] Jones, Whiting, Armitage, Cook, and Entwistle, *Nature*, 1951, **168**, 900.
[2] Allan, Jones, and Whiting, *J.*, 1955, 1862.
[3] Bohlmann and Viehe, *Chem. Ber.*, 1955, **88**, 1017.
[4] Bohlmann and Mannhardt, *ibid.*, p. 429.
[5] Armitage, Jones, and Whiting, *J.*, 1952, 1993.
[6] Cook, Jones, and Whiting, *J.*, 1952, 2883.

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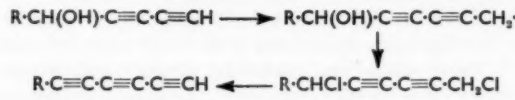
disodio-derivative of hepta-4 : 6-diyn-3-ol with formaldehyde, chlorination, and dehydrochlorination :



Method (*a*) was first re-examined; alkylation of monosodiohexatriyne in liquid ammonia with methyl or ethyl bromide gave a mixture of hexatriyne with its mono- and di-alkylated derivatives, which were isolated by extraction with butane at −78°. Evaporation of the greater part of the solvent was expected to remove the hexatriyne by co-distillation, while the dialkylated hydrocarbons should, of course, be inert to ethylmagnesium bromide. Nevertheless, carboxylation of the hydrocarbon obtained gave, in each case, an unstable acid, which could not be satisfactorily purified and had an ultraviolet spectrum including extraneous bands at *ca.* 3600 and 3850 Å.

The octa-2 : 4 : 6-triynoic acid specimen prepared by this route and reported earlier,[1] though obtained in only *ca.* 1% yield, showed an ultraviolet absorption spectrum in agreement with that described below, without extraneous maxima. It gave octanoic acid on hydrogenation; the reason for our repeated lack of success in reproducing this work is not clear.

Method (*b*) suffers from the disadvantage that the disodium derivatives of acetylenic glycols $RR'C(OH)\cdot[C{\equiv}C]_n\cdot C(OH)RR'$ dissociate reversibly in liquid ammonia,[7] so that the glycol so prepared was probably contaminated with hexa-2 : 4-diyne-1 : 6-diol. However, Grignard condensation of penta-2 : 4-diyn-1-ol,[5] for which a much improved method of preparation was devised, with acetaldehyde or propionaldehyde proved more satisfactory and in the former case gave a crystalline glycol. This readily yielded a homogeneous dichloroheptadiyne, as was to be expected from the behaviour of the two related symmetrical glycols, $R\cdot CH(OH)\cdot[C{\equiv}C]_2\cdot CH(OH)\cdot R$ (R = H or Me).[6] Unpublished work by the authors, however, had shown that when an acetylenic glycol grouping is flanked by alkyl groups higher than methyl, dehydration competes with the replacement of the hydroxyl group by chlorine. The formation of a mixture from octa-2 : 4-diyne-1 : 6-diol was therefore not unexpected. Careful fractionation gave low-boiling material rich in 1-chloro-oct-6-ene-2 : 4-diyne, and the desired 1 : 6-dichloro-octa-2 : 4-diyne in a state of essential purity.

When the two dichloro-compounds were dehydrohalogenated at −78° and the resultant hydrocarbons were carboxylated *via* the Grignard reagents, triacetylenic acids were obtained which could be purified by crystallisation, and were finally obtained free from the impurities responsible for anomalous light-absorption bands. They also proved to be less unstable than the very impure acids isolated previously; rather surprisingly the octatriynoic acid separated from (moist) methylene chloride as a hydrate, analogous to that of its diacetylenic analogue, hexa-2 : 4-diynoic acid.[8]

Esterification of the di- and tri-acetylenic acids was best effected with methanolic sulphuric acid at room temperature. The esters gave relatively stable crystalline amides on treatment with aqueous ammonia. Dehydration of αβ-acetylenic amides[9] with phosphoric oxide at 100—150° proceeds smoothly, and this apparently brutal reaction readily gave a 50% yield of the nitrile of hepta-2 : 4-diynoic acid. It even proved possible to prepare, in small quantity, the nitrile of nona-2 : 4 : 6-triynoic acid. The conjugated di- and tri-acetylenic nitriles are appreciably more stable than the other acid derivatives.

Treatment of methyl hepta-2 : 4-diynoate with diazomethane, piperidine, and *cyclo*pentadiene resulted in the expected additions. In the second case the reaction could be shown to involve the triple bond adjacent to the methoxycarbonyl grouping by comparing

[7] Unpublished work; cf. Burkhardt and Hindley, *J.*, 1938, 987.
[8] Schlubach and Wolf, *Annalen*, 1950, **568**, 141.
[9] Moureu and Lazennac, *Bull. Soc. chim.*, 1906, **35**, 520.

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the ultraviolet absorption spectrum of the product with that of appropriate model substances;[10] and this was assumed to be true in the other cases also.

Ultraviolet spectra of the di- and tri-acetylenic acids, esters, amides, and nitriles are tabulated. The data for the acids agree well with those recorded earlier for the acids $CH_3 \cdot [C \equiv C]_n \cdot CO_2H$;[2,3] these acids are relatively strong, and would probably show deviations from Beer's law, even in 95% ethanol.[2] Thus in the dilute solutions used for

Ultraviolet absorption maxima, in 95% ethanol.

(a) *Diacetylenic acids and their derivatives,* $R \cdot C \equiv C \cdot C \equiv C \cdot COX$

R	X	$\lambda_{max.}$ (Å) (ε) *A*	$\lambda_{max.}$ (Å) (ε) *B*	$\lambda_{max.}$ (Å) (ε) *C*	$\lambda_{max.}$ (Å) (ε) *D*	$\lambda_{max.}$ (Å) (ε) *E*
Et	OH	2755 (2950)	2600 (4250)	2465(3250)	2345 (1800)	2235 (900)
Bu[a]	OH	2760 (2800)	2610 (4300)	2475 (3600)	2345 (2200)	2240 (1300)
Et	OMe	2770 (4000)	2615 (5500)	2480 (4050)	2350 (2250)	2240 (1150)
Et	NH_2	2745 (3750)	2590 (5450)	2455 (4700)	2325 (4550)	2210 (5100)
$Me_2C(OH)$	OH	2745 (3050)	2600 (4450)	2460 (3450)	2325 (1900)	

(b) *Triacetylenic acids and their derivatives,* $R \cdot [C \equiv C]_2 \cdot COX$.

(i) Medium-intensity bands:

R	X	*A*	*B*	*C*	*D*	*E*
Me	OH	3275 (1950)	3065 (2900)	2880 (2400)	2720 (1450)	2575 (800)
Et	OH	3285 (2000)	3070 (3050)	2885 (2450)	2725 (1400)	2580 (700)
Me	OMe	3295 (2700)	3080 (4000)	2895 (3250)	2730 (2000)	2585 (1100)
Et	OMe	3295 (3200)	3085 (4450)	2900 (3500)	2735 (2200)	2585 (1400)
Me	NH_2	3255 (2350)	3045 (3500)	2865 (2800)	2695 (1850)	

(ii) High-intensity bands:

		L	*M*
Me	OH	2195 (102,000)	2110 (72,000)
Et	OH	2210 (115,000)	2115 (95,000)
Me	OMe	2255 (80,000)	2175 (70,000)
Et	OMe	2265 (77,000)	2175 (67,000)
Me	NH_2	2230 (89,000)	2145 (73,000)

(c) *Acetylenic nitriles*:

	A	*B*	*C*	*D*		
$Et \cdot C \equiv C \cdot C \equiv N$	2350 (105)	2230 (210)	2130 (210)	2040 (150)		
cf. $Et \cdot C \equiv C \cdot C \equiv CH$ [a]	2505 (210)	2370 (340)	2255 (300)			
$Me \cdot C \equiv C \cdot C \equiv C \cdot Me$ [a]	2500 (160)	2355 (330)	2240 (360)	2130 (300)		
$Et \cdot [C \equiv C]_2 \cdot CN$	2960 (100)	2775 (165)	2610 (110)	2465 (110)	2330 (85)	2000 (91,000)
cf. $Et \cdot [C \equiv C]_2 \cdot H$ [b]	3050 (90)	2800 (190)	2650 (260)	2510 (250)		
$Me \cdot [C \equiv C]_2 \cdot Me$ [c]	3060 (120)	2860 (200)	2680 (200)	2530 (130)	2390 (105)	2070 (>135,000)

	L	*M*	*N*	*O*
$Et \cdot [C \equiv C]_3 \cdot CN$	2340	2250	2160	2070 (in alcohol)
cf. $H \cdot [C \equiv C]_4 \cdot H$ [d]	2270	2170	2070	(in pentane)
$Me \cdot [C \equiv C]_4 \cdot Me$ [e]	2345	2235	2145	2040 (in alcohol)
$NC \cdot [C \equiv C]_2 \cdot CN$ [f]	2040 (100,000)			(in hexane)

[a] Armitage, Cook, Entwistle, Jones, and Whiting, *J.*, 1952, 1998. [b] Cook, unpublished work; cf. ref. (*d*). [c] Armitage, Cook, Jones, and Whiting, *J.*, 1952, 2010. [d] Cook, Jones, and Whiting, *J.*, 1952, 2883. [e] Armitage, Jones, and Whiting, *J.*, 1952, 2014. [f] Schlögl, unpublished work.

measuring the high-intensity ("*L*, *M* . . .") bands the acids are probably predominantly ionised, whereas in those employed to measure the medium-intensity ("*A*, *B*, *C* . . .") bands this would probably not be the case. On this assumption the results for the acids, esters, and amides are compatible with the general rules that conjugation of C=O with the acetylenic linkages increases in the order $CO_2^- < CO \cdot NH_2 < CO_2H \sim CO_2Me$, and that such conjugation produces the usual increase in the intensities of the *A*-group bands, reduction in those of the *L*-group bands, and bathochromic displacements in both. Bands of the *A*-series in the di- and tri-acetylenic acids are at very much the same positions as (though of lower intensity than) those of the corresponding ethylenic compounds,

[10] Bowden, Braude, Jones, and Weedon, *J.*, 1945, 45.

$[C{\equiv}C]_n{\cdot}CH{=}CH_2$, etc.[11] It is fortunate for diagnosis that the *L*-band-group of the triacetylenic acids and esters are displaced by −140 Å relative to those of the ethylenic systems.

The remarkable bathochromic effect of propargylic hydroxyl groups [12] disappears completely when a carboxyl group is added to the chromophore.

The ultraviolet spectra of the nitriles differ profoundly from those of the other derivatives; this is true for the parent αβ-acetylenic nitriles also, which may be conveniently dealt with here. Clearly cylindrically-symmetrical conjugative interaction takes place with the consequence that $-[C{\equiv}C]_n{\cdot}C{\equiv}N$ resembles $[C{\equiv}C]_{(n+1)}$, showing the characteristic absorption spectra of simple poly-ynes with two band-systems of very different intensities. Indeed, the intensities of absorption of the acetylenic nitriles are even lower, in the long-wavelength region, than those of the poly-ynes themselves, and might easily escape detection during, *e.g.*, examination of biological material. Dicyanobutadiyne shows essentially similar behaviour.

The infrared spectra of the acids and esters have already been discussed.[13] Simple acetylenic nitriles show two strong bands at *ca.* 2270 and 2320 cm.$^{-1}$, while the diacetylenic nitrile have a broader band at 2235 cm.$^{-1}$.

Experimental

Hepta-2 : 4-diynoic Acid.—A solution of hepta-1 : 3-diyne (17·5 g.) in ether (35 c.c.) was added dropwise to ethylmagnesium bromide (from 10 g. of magnesium) in ether (*ca.* 200 c.c.). The mixture was heated under reflux for 1 hr. and poured on an excess of powdered carbon dioxide in an autoclave of capacity 1·4 l. After 18 hr. the excess of carbon dioxide was released and the complex was decomposed with ice and 15% sulphuric acid. Isolation of the acidic fraction gave a solid, which was crystallised several times from light petroleum (b. p. 40—60°), yielding the *acid* (13·5 g., 50%), m. p. 73—75° (Found : C, 67·9; H, 4·65. $C_7H_6O_2$ requires C, 68·8; H, 4·9%). The *methyl ester*, prepared either with diazomethane or in methanolic sulphuric acid, had b. p. 50°/0·01 mm., $n_D^{17\cdot5}$ 1·5131 (Found : C, 71·3, 69·3; H, 5·2, 5·8. $C_8H_8O_2$ requires C, 70·6; H, 5·9%).

Nona-2 : 4-diynoic Acid.—Prepared similarly from octa-1 : 3-diyne (21 g.) and magnesium (6 g.), this *acid* (12·3 g., 40%) formed needles, m. p. 32—37°, from pentane (Found : C, 72·2; H, 6·85. $C_9H_{10}O_2$ requires C, 72·0; H, 6·7%).

Penta-2 : 4-diyn-1-ol.—(Improved method.) 1 : 4-Dichlorobut-2-yne (74 g.) was added with stirring to a suspension of sodamide, prepared in a vacuum-flask from sodium (41 g.) in liquid ammonia (1·1 l.). Ether (100 c.c.) and, during 10 min., a suspension of dried paraformaldehyde (18 g.) in ether (100 c.c.) were added. After 1 hr. ammonium chloride (80 g.) was added, the suspension was transferred to a beaker with the aid of more ether, and the bulk of the ammonia was allowed to evaporate. The solution was filtered, and the solids were well washed with ether; the filtrate was evaporated to half its volume to remove the rest of the ammonia, then dried ($MgSO_4$) and evaporated further, finally under reduced pressure at room temperature. The residue was extracted with light petroleum (b. p. 40—60°; 500 c.c.), which was evaporated, finally at 0·01 mm. at room temperature, leaving a red oil (47 g., 65%), n_D^{20} 1·521—1·522, which solidified completely and was sufficiently pure for further work. Experience has shown that distillation of this alcohol at 60—80°/0·01 mm. is both wasteful and hazardous (cf. ref. 5).

Hepta-2 : 4-diyne-1 : 6-diol.—A solution of ethylmagnesium bromide was prepared from magnesium (17 g.) in ether (300 c.c.), and benzene (320 c.c.) was added slowly while the ether was distilled off. A solution of penta-2 : 4-diyn-1-ol (21 g., as above) in benzene (170 c.c.) was added with ice-cooling. After 40 min. acetaldehyde (18 g.) in benzene (50 c.c.) was added, and the mixture was stirred for a further 18 hr. The complex was decomposed with ice and water, the benzene layer was separated without filtration, and the aqueous layer was extracted continuously for 18 hr. The combined extracts were dried ($MgSO_4$) and evaporated; the

[11] Bohlmann and Viehe, *Chem. Ber.*, 1954, **87**, 712.
[12] Armitage and Whiting, *J.*, 1952, 2005.
[13] Allan, Meakins, and Whiting, *J.*, 1955, 1874.

residue was dissolved in benzene and adsorbed on alumina, and the benzene–ether eluates were distilled at 85° (bath-temp.)/5×10^{-4} mm., after which the *glycol* (11 g., 33%) crystallised and had m. p. 50—53° after recrystallisation from ether (Found: C, 67·45; H, 6·55. $C_7H_8O_2$ requires C, 67·7; H, 6·45%).

Octa-2 : 4-diyne-1 : 6-diol was prepared similarly from penta-2 : 4-diyn-1-ol (26 g.), magnesium (20 g.), and propionaldehyde (30 g.). Chromatography and distillation at 100° (bath-temp.)/0·02 mm. gave a yellow oil (25 g., 56%), n_D^{21} 1·5370, $\lambda_{max.}$ 2310 Å (ε 1050), which was chlorinated without further purification.

1 : 6-*Dichlorohepta*-2 : 4-*diyne*.—Hepta-2 : 4-diyne-1 : 6-diol (10 g.) and pyridine (13·5 c.c.) were treated below 30° with thionyl chloride (14·7 c.c.), added dropwise. After being stirred for 18 hr. the mixture was poured on ice, and the neutral product was isolated. Distillation gave the *dichloride* (4·5 g., 35%), b. p. 31°/0·01 mm., n_D^{19} 1·5530 (Found: C, 52·95; H, 4·55; Cl, 42·8. $C_7H_8Cl_2$ requires C, 52·2; H, 3·7; Cl, 44·1%), shown by its ultraviolet absorption spectrum to be essentially pure (max. at 2670, 2520, 2390, and 2270 Å; ε 1350, 2050, 1650, and 1100, respectively; no absorption band at longer wavelengths).

1 : 6-*Dichloro-octa*-2 : 4-*diyne*.—Octa-2 : 4-diyne-1 : 6-diol (23 g.) and pyridine (35 c.c.) were treated with thionyl chloride (31 c.c.) below 30°. After being stirred for 15 hr. the dark mixture was poured on ice, and the neutral product was isolated with ether and distilled, giving a crude product (16 g.), n_D^{20} 1·5518—1·5441. Careful fractionation gave the essentially pure *dichloro-compound*, b. p. 60°/0·01 mm., n_D^{23} 1·5457 (Found: C, 55·25; H, 4·85. $C_8H_8Cl_2$ requires C, 55·0; H, 4·6%); absorption max. at 2670, 2520, 2390, and 2260 Å (ε 1450, 2250, 1850, and 1450, respectively). The first fraction had $n_D^{19\cdot5}$ 1·5703, showed absorption maxima at 2890, 2830, 2730, 2650, 2540, 2535, and 2400 Å ($E_{1\,cm.}^{1\%}$ 320, 370, 500, 510, 380, 400, and 260, respectively), and thus contained *ca.* 30% of 1-chloro-oct-6-ene-2 : 4-diyne.

Nona-2 : 4 : 6-*triynoic Acid*.—1 : 6-Dichloro-octa-2 : 4-diyne (2 g.) in ether (3 c.c.) was added dropwise during 10 min. to a suspension of sodamide, prepared from sodium (0·6 g.) and liquid ammonia (30 c.c.) and previously cooled to −77° by direct addition of liquid nitrogen; more of the latter was added during the reaction. The mixture was kept for 20 min., then ammonium chloride was added in excess. The liquid ammonia solution was extracted with *iso*butane (4 × 100 c.c.), and the extract was evaporated to 50 c.c. under reduced pressure in the presence of magnesium sulphate. After filtration tetrahydrofuran (50 c.c.) was added, and evaporation was continued until the total volume was 15 c.c.; the solution of octa-1 : 3 : 5-triyne was then added at 0° to a solution of ethylmagnesium bromide, prepared from magnesium (0·5 g.) in tetrahydrofuran. The mixture was stirred for 30 min. at 15°, then poured on a large excess of solid carbon dioxide in an autoclave. After 18 hr., excess of carbon dioxide was released and the complex was decomposed with ice-cold 15% sulphuric acid. The acidic fraction was separated with ether *via* potassium hydrogen carbonate solution. After drying ($MgSO_4$) the dark ethereal extract was reduced in volume to 5 c.c., and carefully treated with pentane at 15°, which precipitated tar, leaving a clear orange solution. Evaporation at 15° gave a brown crystalline residue which was dissolved in methylene dichloride (3·5 c.c.); on cooling to −70°, crystals separated. After three further crystallisations from methylene dichloride, *nona*-2 : 4 : 6-*triynoic acid* (160 mg., 10%) formed long pale-yellow needles, decomp. 95° (Found: C, 73·8; H, 4·2. $C_9H_6O_2$ requires C, 73·95; H, 4·15%). A further quantity of less pure material was isolated from the mother-liquors.

Octa-2 : 4 : 6-*triynoic Acid*.—1 : 6-Dichlorohepta-2 : 4-diyne (2 g.) was dehydrohalogenated, by an essentially similar technique, to hepta-1 : 3 : 5-triyne, which was added to ethylmagnesium bromide (from 0·6 g. of magnesium) in tetrahydrofuran. Carboxylation, isolation of the acidic material, precipitation of tar by pentane from ether, and crystallisation from methylene dichloride at −70° gave *octatriynoic acid monohydrate* (0·2 g.) (Found: C, 63·8, 65·0; H, 4·3, 4·1. $C_8H_4O_2,H_2O$ requires C, 64·0; H, 4·0. $C_8H_4O_2$ requires C, 72·7; H, 3·0%). The *methyl ester*, obtained by the action of 3% methanolic sulphuric acid for 4 days at 15°, formed needles, m. p. 53—56°, from light petroleum (Found: C, 75·05; H, 5·5. $C_9H_6O_2$ requires C, 74·0; H, 4·15%). (Bohlmann and Viehe [3] give m. p. 157°, which is believed to be a misprint.)

Hepta-2 : 4-*diynamide*.—Methyl hepta-2 : 4-diynoate (1·1 g.) and ammonia solution (*d* 0·88; 10 c.c.) were shaken for 3·5 hr. at 15°. The *amide* (0·6 g.) was collected, dried, and crystallised from benzene–ethanol as leaflets, m. p. 148° (Found: C, 69·5; H, 5·9; N, 11·75. C_7H_7ON requires C, 69·4; H, 5·8; N, 11·5%).

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Octa-2 : 4 : 6-triynamide.—Methyl octa-2 : 4 : 6-triynoate (170 mg.) was triturated with ammonia solution (*d* 0·88; 2·5 c.c.) at −5°. The mixture was warmed to 15° for 2 hr., with exclusion of light, and the product was isolated with ether. After crystallisation from tetrahydrofuran–methylene dichloride the *amide* formed needles (70 mg.), discoloring at 85° (Found : C, 72·2, 72·05; H, 4·1, 4·35; N, 10·4. C_8H_5ON requires C, 73·3; H, 3·8; N, 10·7%).

Hepta-2 : 4-diynonitrile.—Hepta-2 : 4-diynamide (1·0 g.), sand (1·5 g.), and phosphoric oxide (2 g.) were heated at 100—130°/0·01 mm. in a cold-finger sublimation apparatus. The sublimate was allowed to warm to 15°; it liquefied; it was dissolved in pentane (5 c.c.) and shaken with saturated aqueous potassium carbonate, to remove acidic impurities, dried, and evaporated at −5°. Sublimation of the residue at 20°/0·01 mm. gave the *nitrile* (400 mg.), m. p. *ca.* −5°, n_D^{23} 1·5387 (Found : C, 81·0; H, 5·25; N, 13·6. C_7H_5N requires C, 81·5; H, 4·9; N, 13·6%).

Nona-2 : 4 : 6-triynonitrile was prepared from the acid (90 mg.) *via* the ester and amide in the same way without isolation of intermediates; the sublimed product was at once dissolved in ethanol for an examination of its ultraviolet absorption spectrum, tabulated above.

Adducts of Methyl Hepta-2 : 4-diynoate.—(a) *With diazomethane.* The ester was treated with an excess of diazomethane in ether during 24 hr. at room temperature. The solution was evaporated, and the residue was crystallised several times from benzene–light petroleum, giving *methyl 4-but-1′-ynylpyrazole-3-carboxylate*, m. p. 92—94° (Found : N, 15·7. $C_9H_{10}O_2N_2$ requires N, 15·7%). Light absorption : max. 2405 Å, infl. 2435 and 2615 Å (ε 10,600, 10,400, and 6600); and in the infrared, strong bands at 3200—3400 and 1727 cm.$^{-1}$ and a weak band at 2250 cm.$^{-1}$.

(b) *With piperidine.* Piperidine (1·33 g.) in ethanol (11 c.c.) was added slowly to a solution of the ester (2 g.) in ethanol (11 c.c.); the temperature rose to 30°. After 18 hr. evaporation of the solvent and distillation gave *methyl 3-1′-piperidylhept-2-en-4-ynoate*, b. p. 140° (bath-temp.)/10^{-4} mm., n_D^{17} 1·5551 (Found : C, 71·5; H, 9·1; N, 6·25. $C_{13}H_{19}O_2N$ requires C, 70·7; H, 9·6; N, 6·3%). Light absorption : max. 2320 and 3090 Å (ε 6700 and 14,700); and in the infrared, strong bands at 2247 and 1706 cm.$^{-1}$, medium band at 1630 cm.$^{-1}$.

(c) *With* cyclo*pentadiene.* The ester (2·3 g.) and *cyclo*pentadiene (2·3 g.) were heated in a sealed tube at 95° for 3 hr. After 18 hr. at 20° the crude product was extracted with light petroleum (b. p. 40—60°). Evaporation of the solvent and distillation gave *methyl 2 : 5-dihydro-2 : 5-endomethylene-6-but-1′-ynylbenzoate* (0·7 g.), b. p. 71° (bath temp.)/0·01 mm., n_D^{23} 1·5335 (Found : C, 76·35; H, 6·9. $C_{13}H_{14}O_2$ requires C, 77·2; H, 7·0%). Light absorption : max. 2915 Å (ε 6220); and in the infrared a weak band at 3070 cm.$^{-1}$ (*cis*-CH=CH stretching), medium-intensity bands at 2245 and 2215 cm.$^{-1}$, and strong bands at 1707 and 720 cm.$^{-1}$.

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387. *Metal Carbonyl Compounds. Part III.* Reactions of Monocarbonyl Complexes of Platinum*(II).

By R. J. Irving and E. A. Magnusson.

The reaction of neutral monodentate ligands with the dimeric carbonyl halides of platinum gives rise to compounds $\{Pt(CO)LX_2\}$ whose stabilities and configurations are generally dependent on the *trans*-effect of the ligands introduced. Very weakly π-bonding ligands (ammonia or *p*-toluidine) in excess do not easily expel carbon monoxide, but addition of excess of the more strongly bonding ligands (pyridine or phosphorus trichloride) results in immediate evolution of carbon monoxide, even at low temperatures. The introduction of strongly double-bonding bidentate ligands such as *o*-phenylenebisdimethylarsine results in the rapid elimination of carbon monoxide, though the transitory existence of the entity containing both ligands can be demonstrated.

Reaction mechanisms are discussed, on the basis of which the general behaviour of halogen-bridged platinum compounds may be explained.

It is now generally agreed that "*trans*-effect" in Pt(II) complexes is largely determined by the character of the bond between the ligand and the platinum atom.[1-3] With ligands such as carbon monoxide, ethylene, phosphorus trifluoride, and, perhaps to a smaller extent, phosphorus trichloride, π-bonding (back-co-ordination between the filled *d*-orbitals of platinum and the unfilled *p*- or *d*-orbitals of the co-ordinating atom) accounts for much of the bond strength.[2,3] In ligands such as mono- or di-tertiary arsines, these π-bonds exist in addition to stronger σ-bonds. The *d*-orbitals responsible for this co-ordination have been qualitatively represented by Chatt and Duncanson.[3] In the case of redistribution of overlap caused by competition for π-character by two ligands *trans* to each other, labilisation of the ligands not stabilised by strong σ-overlap will occur. Accordingly, we may expect arsines and other strong "double-bonding" † ligands to labilise ligands such as carbon monoxide and ethylene, but not to be labilised to any great extent by them.

The purpose of this section of the investigation has been to study the action of ligands possessing varying degrees of "*trans*-effect" on the dimeric carbonyl platinous halides described in Part I. The probable schemes of reaction are outlined below (L = monodentate ligand; L–L = bidentate ligand; X = Cl, Br, or I).

Where L is ammonia, compounds (II), (III), and (IV) have been isolated.[4,5] The compounds (II; L = *p*-toluidine, pyridine, or methyldiphenylarsine) are relatively stable to heat but sensitive to moisture; of these the *p*-toluidine compound is by far the most stable to heat and moisture, and also in the presence of excess of ligand. Isolation of the salt (III) was not possible in the case of pyridine and methyldiphenylarsine. The action

* Parts I and II (*J.*, 1956, 1860, 2879) were published under a different general title.

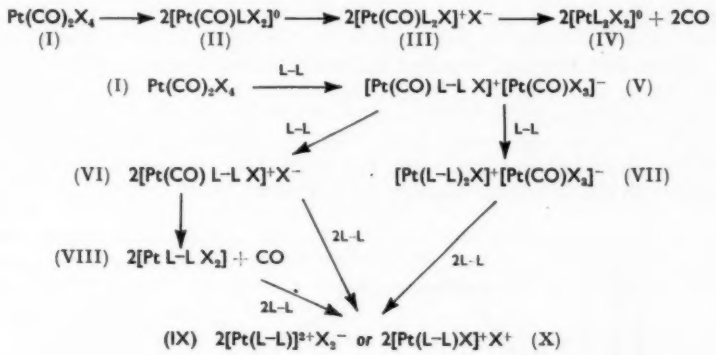
† The term "double-bonding ligand" indicates a ligand which possesses a strong σ-bond and also a strong π-bond. The terms "π-bonding ligand" and "σ-bonding ligand" refer to ligands which form bonds deriving their strength mainly from π-bonds and σ-bonds respectively. This distinction between the σ-bond strengths of ligands possessing π-bonds in addition is important in discussions of stabilities and of directive effects in complex compounds. Thus the "*trans*-directing" properties of the ligands CO, PCl_3, PF_3, C_2H_4, methyldiphenylarsine, and *o*-phenylenebisdimethylarsine ("Diarsine") are all fairly high, but the relative stabilities of platinum(II) compounds involving these ligands differ markedly with respect to heat, moisture, and excess of ligand.

[1] Emeléus and Anderson, "Modern Aspects of Inorganic Chemistry," Routledge and Kegan Paul, London, 1952, pp. 413, 418.
[2] Chatt and Williams, *J.*, 1951, 3061.
[3] Chatt and Duncanson, *J.*, 1953, 2939.
[4] Schutzenberger, *Bull. Soc. chim.*, 1870, **14**, 97.
[5] Gelman, *Ann. Inst. Plat.*, 1945, **18**, 50.

of excess of these ligands on compound (II) immediately liberated carbon monoxide and formed compound (IV) even below −30°.

In view of the foregoing, phosphorus trichloride would also be expected to form a compound of type (II). Emeléus and Anderson [1] reported that the action of two mols. of phosphorus trichloride removed all the carbon monoxide from the dimer. The present work supports this, but by the action of one mol. it is possible to isolate very unstable carbonyl-containing compounds (II), the bromide and iodide being isolated in the pure state. The chloride could not be freed from impurity but a comparison of its infrared spectrum with those of the bromide and iodide strongly supported its identity (see Part I).

The action of phosphorus trichloride was studied conductometrically in dry acetone at 0°. After addition of more than one mol. per platinum atom, carbon monoxide was evolved. No evidence of even transitory salt formation was observed. Pyridine behaved in the same way.


Pt(CO)2X4 → 2[Pt(CO)LX2]0 → 2[Pt(CO)L2X]+X− → 2[PtL2X2]0 + 2CO
(I) (II) (III) (IV)
(I) Pt(CO)2X4 L–L [Pt(CO) L–L X]+[Pt(CO)X3]− (V)
L–L L–L
(VI) 2[Pt(CO) L–L X]+X− [Pt(L–L)2X]+[Pt(CO)X3]− (VII)
(VIII) 2[Pt L–L X2] + CO
2L–L 2L–L 2L–L
(IX) 2[Pt(L–L)]2+X2− or 2[Pt(L–L)X]+X+ (X)

Dipyridyl forms compounds (V) and (VI) which are stable in dry air. In the presence of moisture and excess of ligand, compounds (VIII) and (IX) respectively are formed with the liberation of carbon monoxide. The action of *o*-phenanthroline is analogous.

When *o*-phenylenebisdimethylarsine (" Diarsine ") was used, no carbonyl-containing entities could be isolated but compounds with the 5-covalent cation $[Pt(Diarsine)_2X]^+$ were always obtained, even at −50°. The labilisation of carbon monoxide due to the strong " double-bonding " of the diarsine is such that the intermediate compound (V) must be very unstable. Colour changes during the reaction suggested its formation and this was supported by conductivity titrations. Table 1 shows the C–O stretching frequencies of substances isolated in attempts to prepare diarsine carbonyl compounds. No absorption

TABLE 1.

Starting material	Frequency (cm.$^{-1}$) of absorption peak after reaction with diarsine	Assignments [a]
$[Pt(CO)Cl_3]_2$	2105	$[Pt(CO)Cl_3]^-$
$[Pt(CO)Br_3]_2$	2092	$[Pt(CO)Br_3]^-$
$[Pt(CO)I_3]_2$	2082	$[Pt(CO)I_3]^-$

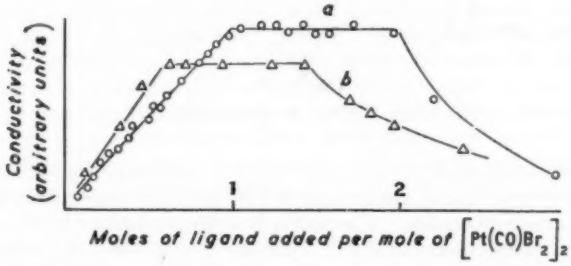
[a] Irving and Magnusson, *J.*, 1956, 1860.

indicative of carbon monoxide in a co-ordination entity containing diarsine was obtained.

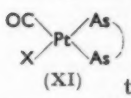
As Diarsine was added to a solution of $(PtCOBr_2)_2$ in dry acetone at 0° (Fig. *a*), the conductivity of the solution increased linearly, reaching a maximum after the addition of one mole of ligand per mole of dimer. This point corresponds to the formation of compound (V). Addition of more ligand resulted in slow evolution of carbon monoxide but

did not greatly affect the conductivity until 2 mol. had been added, after which the conductivity slowly decreased. This decrease was accompanied by the further evolution of carbon monoxide and precipitation of the salt (X). At room temperatures, the conductivity curve followed the same trend but the salt (X) began to be precipitated well before 2 equivs. of ligand had been added (Fig. *b*). The sequence (I)–(V)–(VII)–(X) represents a possible course of reactions on the basis of the above evidence. If the initial attack is in the CO–Pt direction rather than along the bridging halogen–Pt bond, carbon monoxide would be given off immediately irrespective of temperature. The compounds (X) were identified with those obtained by Harris, Nyholm, and Stephenson.[6] The short Pt–As bond distance (2·38 Å) noted by these authors, and their postulate of double-bonding, explain the strong labilising properties attributed to Diarsine in the reactions described above. The compounds (VII) are quite stable and may be isolated by the action of Diarsine on (I) or on the ions $[Pt(CO)X]_3^-$. The alternative scheme (I)–(V)–(VI)–X is thus eliminated.

It is well known that addition of potassium cyanide to any platinum carbonyl compound results in the evolution of carbon monoxide with the formation of the tetracyano-complex. Mylius and Foerster [7] reported that the addition of aqueous potassium cyanide to the hydrochloric acid solution of $[Pt(CO)Cl_2]_2$ produced a colour change suggesting the formation of intermediates $Pt(CO)(CN)_2$ or $K[Pt(CO)(CN)_3]$ before formation of $K_2Pt(CN)_4$, but they could not isolate these compounds. We attempted to isolate a carbonyl cyanide compound at temperatures down to −40°, but in all cases evolution of carbon monoxide was immediate and the compound isolated was $K_2Pt(CN)_4$.



Properties of the Derivatives (II).—Physical properties of the co-ordination compounds $[Pt(AsMePh_2)(CO)X_2]$ point to the *cis*-configuration. These compounds are comparatively stable, paler than their *p*-toluidine analogues, and not appreciably soluble in non-polar solvents. Further, their C–O stretching frequencies are not far removed from those of the entities $[Pt(CO)X_3]^-$, whereas C–O frequencies for the *trans*-$[Pt(CO)\ p\text{-tol}X_2]$ are higher by about 30 cm.$^{-1}$ (X = Cl, Br, and I). Further support for this configuration is supplied by the fact that the C–O stretching frequencies of $[Pt(AsMePh_2)(CO)Cl_2]$ and of the compound believed to be $[Pt(AsMePh_2)_2(CO)Cl]^+Cl^-$ [*trans*-di(methyldiphenylarsine)carbonylchloroplatinum(II) chloride] are almost identical. Chatt and Wilkins [8] have shown that the *cis*-forms of the compounds $PtLL'X_2$ are more stable than the *trans*-forms when both L and L′ have appreciable *trans*-effect, and the instability of the entity (XI) is in agreement with this. *cis*-Planar compounds containing two double-bonding ligands are expected to be more stable than the corresponding *trans*-isomers.[9-11]



(XI)

[6] Harris, Nyholm, and Stephenson, *Nature*, 1956, **177**, 1127.
[7] Mylius and Foerster, *Ber.*, 1891, **24**, 2426; Foerster, *ibid.*, p. 3751.
[8] Chatt and Wilkins, *J.*, 1952, 273.
[9] Jaffe, *J. Phys. Chem.*, 1954, **58**, 185.
[10] Craig, Maccoll, Nyholm, Orgel, and Sutton, *J.*, 1954, 332.
[11] Chatt and Wilkins, *J.*, 1952, 4300.

Phosphorus trichloride has empty 3*d*-orbitals available for π-bonding and should have a similar *trans*-effect to the tertiary arsines and phosphines. It might also be expected to form stable compounds of *cis*-configuration. However, its compounds are very unstable, quite soluble in non-polar solvents, have C–O frequencies 30—40 cm.$^{-1}$ higher than those for compounds with CO *trans*- to halogen {*e.g.*, $[Pt(CO)X_3]^-$ or *cis*-$Pt(CO)LX_2$}, and are more brightly coloured. This suggests *trans*-configuration.

Attempts to prepare the *trans*-arsine compounds $Pt(AsMePh_2)(CO)X_2$ by the action of methyldiphenylarsine on the ion $[Pt(CO)X_3]^-$ were unsuccessful, carbon monoxide being evolved on all occasions. Also, attempted substitution by the arsine in hot acetone solutions of the dimers $[Pt(CO)X_2]_2$ resulted in decomposition, presumably because of dissociation. On the other hand, ligands less strongly *trans*-labilising than the arsine readily form *trans*-compounds in the reaction with the single entity $[Pt(CO)X_3]^-$. This is paralleled by the action of amines on Zeise's salt.[12] Indeed, pyridinium carbonyltri-iodoplatinite [13] forms the compound *trans*-pyridinecarbonyldi-iodoplatinum(II) on storage. It is apparent that a different mechanism is involved in the formation of derivatives by bridge fission of the dimeric compounds from that in the reaction with the ion $[PtLX_3]^-$, at least in the case where the directing ligand L and the entering ligand L′ are both of fairly high *trans*-effect.

Discussion of Mechanisms.—Previous discussions (for references see Chatt [14]) give no detail, and *trans*-bridge fission is the only possibility considered. However, the formation of *cis*- or *trans*-compounds, or equilibrium mixtures of both, from halogen-bridged dimers $[PtLX_2]_2$ by the action of any neutral ligand L′ will probably involve one of the following mechanisms: (i) Initial formation of *trans*-compounds by *trans*-bridge fission, with subsequent possible isomerisation to *cis*. (ii) Direct formation of *trans*- or *cis*-compounds after fission of the *trans*- or *cis*-bridges, respectively. (iii) Formation of intermediates from which the *cis*- or *trans*-products may result, depending on the nature of the orbitals available to the ligands L and L′.

Case (i) probably explains the formation of Rosenheim and Levy's *cis*- and *trans*-compounds,[15] but on this basis the same products would be obtained from the monodentate entity.

Determinations of structure by *X*-ray methods [16, 17] indicate that application of case (ii) must be restricted when the directing ligand L has a high *trans*-effect, owing to the appreciable *trans*-bond weakening in dimeric as well as monomeric compounds.

Case (iii) is more in agreement with recent theories of substitution [6, 18–21] as well as chemical evidence, and involves successive addition of the entering ligands L′ to the "fifth positions" of the configurations. Displacement of the bridge atoms (probably *trans*-displacement for the case where L has a high *trans*-effect) leads to approximately tetrahedral 4-covalent entities from which the *trans*- (normally the more stable) or the *cis*-square planar derivatives (favoured when both L and L′ are π-bonding ligands) may result. The distinction between this mechanism and that of case (i) lies, of course, in the fact that the case (i) rearrangement is the normally slow "isomerisation," whereas that of case (iii) would be expected to be fast. Further, although monomeric substitution will proceed through a somewhat similar initial transition state, the square planar configuration is more nearly retained throughout, resulting in the replacement of the *one* weakly bonded atom,[17] whereas the two weak bridges [16] in the dimer permit the severe

[12] Chatt, Duncanson, and Venanzi, *J.*, 1955, 4461.
[13] Irving and Magnusson, *J.*, 1956, 1860.
[14] Chatt, *J.*, 1951, 652.
[15] Rosenheim and Levy, *Z. anorg. Chem.*, 1905, **43**, 35.
[16] Dempsey and Baenziger, *J. Amer. Chem. Soc.*, 1955, **77**, 4984; Holden and Baenziger, *ibid.*, p. 4987.
[17] Mellor and Wunderlich, *Acta Cryst.*, 1954, **7**, 130; 1955, **8**, 57.
[18] Nyholm, *J. Roy. Inst. Chem.*, 1956, **80**, 328.
[19] Chatt, Duncanson, and Venanzi, *Chem. and Ind.*, 1955, 749; *J.*, 1955, 4456.
[20] Cardwell, *Chem. and Ind.*, 1955, 422.
[21] Ingold, *Chem. Soc. Special Publ.* No. 1, 1954, p. 10.

XUM

distortion of the entities after bridge fission. Experimentally, for L = CO, all reactions are fast whether *cis*- or *trans*-products result, whereas normal *cis*-substitution is slow. The possibility that the ligands L′ " change places " with the bridging atoms before separation of the entities (*i.e.*, with the halogens occupying the fifth positions), and that the *cis*- or *trans*-products result without deformation of the plane, by the bonding of the ligands

TABLE 2.

	Reaction with the dimers $[Pt(CO)X_2]_2$			Reaction with the ions $[Pt(CO)X_3]^-$
Ligand	Products	Stability in air	Stability to excess ligand	
p-Toluidine [13]	(II) (*trans*)	Fairly stable	CO slowly evolved	As with the dimers
Aniline [23], *m*-Nitroaniline [23]	(II) *trans*)	,,	,, ,,	As with the dimers
Ammonia [4]	(II) (*trans*)	,,	(III), (IV) easily formed	As with the dimers [24, 4]
Pyridine	(II) (*trans*)	,,	Immediate evolution of CO; ⟶ (IV)	As with the dimers [24, 4, 5]
$AsMePh_2$ [13]	(II) (*cis*)	,,	Immediate evolution of CO; ⟶ (IV)	Immediate evolution of CO
PCl_3	(II) (*trans*)	Very unstable	Immediate evolution of CO; ⟶ (IV)	—
Carbon monoxide [2]	(II) (*cis*)	Unstable	—	—
	$Pt(CO)_2Cl_2$	Stable in very dry conditions		
Ethylene [4]	(II) (*cis*)	Unstable	—	—
Dipyridyl [13], *o*-Phenanthroline	(V), (VI)	Fairly stable	Strong action gives (VIII), (IX)	As with the dimers
o-$C_6H_4(AsMe_2)_2$	(V), (VII), (X)	Transitory existence only	Almost immediate precipitation of (X)	As with the dimers
Cl^-	$[Pt(CO)Cl_3]^-$	Fairly stable as salt of organic cations. Stable in solution only when excess Cl^- present		
Br^-	$[Pt(CO)Br_3]^-$	Ditto		
I^-	$[Pt(CO)I_3]^-$	More stable to moisture, less stable to heat, than above		
CNS^-	$[Pt(CO)(CNS)_3]^-$ ⟶ $[Pt(CO)(CNS)_4]^=$	Unstable		
CN^-	$K_2Pt(CN)_4$	No carbonyl compounds		

to the most favourable sites on either platinum atom, has been suggested, but the scheme is open to criticism.

With bidentate ligands there is no doubt of the configuration of the products. Previous discussions of such reactions are summarised by Chatt.[14] Attack must take place in the fifth position with the subsequent formation of 5-covalent intermediates. (It should be noted that dipyridyl, *o*-phenanthroline, Diarsine, and other bidentate ligands cannot co-ordinate through one point alone,[22] and any mechanism involving simultaneous attack of the two platinum atoms by one ligand is untenable because of steric effects, for these three compounds at least.) If L′–L′ is a strongly double-bonding ligand such as Diarsine, the intermediate will be unstable. Reaction of bidentate ligands with the ions $[Pt(CO)X_3]^-$ will obviously produce the same results as with the dimers.

In Table 2 the products of reaction of ligands with the platinum carbonyl halides are tabulated in the approximate order of increasing *trans*-effect of the ligands.

[22] Quagliano and Schubert, *Chem. Rev.*, 1952, **50**, 201.

Experimental

Attempted Preparation of Carbonyl-containing Diarsine Compounds.—Chlorine compounds. *o*-Phenylenebisdimethylarsine ("Diarsine") (0·20 g.) in benzene (30 ml.) was added to dicarbonyldichloro-μμ′-dichlorodiplatinum(II) (0·21 g.) in benzene (100 ml.). An immediate yellow-green precipitate was obtained which quickly changed to a deeper yellow. Metallic platinum was slowly precipitated, indicating that not all the dimer had reacted. When 4 moles of diarsine per platinum atom were used precipitation of the yellow derivative was quantitative, no metallic platinum being obtained after the reaction had occurred. The identical yellow precipitate and accompanying colour change were obtained when pyridinium carbonyltrichloroplatinite was used instead of the dimer. The experiment was repeated several times with both starting materials at temperatures down to −50° in the case of the $[Pt(CO)Cl_3]^-$ ion (dissolved in acetone), but it was not possible to isolate any carbonyl-containing entity for any period of time.

Bromine compounds. Diarsine (0·102 g.) in benzene (30 ml.) was added to dicarbonyldibromo-μμ′-dibromodiplatinum(II) (0·138 g.) in benzene (100 ml.). An immediate yellow-orange precipitate quickly gave off bubbles of carbon monoxide, changing colour slightly. The substance dissolved easily in nitrobenzene, and in a M/1000-solution its conductivity was 30·3 mho (calculated on a molecular weight of 1338 for the compound $[Pt(Diarsine)_2Br]^+[Pt(CO)Br_3]^-$). The infrared spectrum of the compound pointed to the presence of the ion $[Pt(CO)Br_3]^-$, the absorption being at 2092 ± 2 cm.$^{-1}$ for a number of experiments. Addition of two more mols. of Diarsine (0·102 g.) produced the yellow substance later shown to be di-(*o*-phenylenebisdimethylarsine)bromoplatinum(II) bromide. Low-temperature reactions with the dimer and the carbonyltribromoplatinite ion again resulted in slower colour changes, but no compounds could be isolated.

Iodine compounds. Reactions with Diarsine yielded results analogous to those described above. The carbonyl-containing complex (assumed to be $[Pt(Diarsine)_2I]^+[Pt(CO)I_3]^-$) absorbed sharply in the infrared region at 2085 cm.$^{-1}$, and further action on this compound produced the 5-covalent salt described below.

A 1 mm. liquid cell with rock-salt windows, so designed as to be easily filled or flushed with solvent, was half-filled with 2% carbon tetrachloride solutions of the respective halogen-bridged carbonyl dimers and cooled to its freezing point. After the cell had been quickly transferred to the cell-holder in the beam of the infrared spectrometer, a solution of Diarsine was added from the filling micropipette (less than one mole of Diarsine per platinum atom being added), and the region 2200—2000 cm.$^{-1}$ quickly scanned. In several instances weak bands were obtained which disappeared after a short time, but in no case were these considered adequate for any serious attempt at assignment.

Di-(o-phenylenebisdimethylarsine)chloroplatinum(II) Chloride.—Diarsine in acetone was added to a solution of platinous carbonyl chloride in concentrated hydrochloric acid until the final yellow precipitate ceased to be formed. The compound may also be prepared by addition of Diarsine in benzene to a benzene solution of the platinous carbonyl chloride dimer. In M/1000-nitrobenzene solution the conductivity was 28·3 mho (Found: C, 28·3; H, 3·8; Pt, 23·4. Calc. for $C_{20}H_{32}As_4Cl_2Pt$: C, 28·6; H, 3·85; Pt, 23·3%).

Di-(o-phenylenebisdimethylarsine)bromoplatinum(II) Bromide.—Diarsine (0·35 g.) in benzene (100 ml.) was added to platinous carbonyl bromide (0·200 g.) in benzene (100 ml.), and the resulting yellow precipitate was filtered off and washed with benzene. In M/1000-nitrobenzene solution the conductivity was 32·0 mhos (Found: C, 25·6; H, 3·3. Calc. for $C_{20}H_{32}As_4Br_2Pt$: C, 25·9; H, 3·5%).

Di-(o-phenylenebisdimethylarsine)iodoplatinum(II) Iodide.—Diarsine (0·50 g.) in benzene (50 ml.) was added to platinous carbonyl iodide (0·30 g.) in benzene (100 ml.). The yellow precipitate was filtered off, washed with benzene, and dried under vacuum (yield approx. 0·7 g.). In M/1000-nitrobenzene solution the conductivity was 28·2 mhos (Found: C, 23·7; H, 3·3; Pt, 20·1. Calc. for $C_{20}H_{32}As_4I_2Pt$: C, 23·5; H, 3·1; Pt, 19·1%).

Attempted Preparation of (Trichlorophosphine)carbonyldichloroplatinum(II).—Phosphorus trichloride (0·20 g.) in carbon tetrachloride (50 ml.) was added to platinous carbonyl chloride (0·29 g.) in carbon tetrachloride (100 ml.). No colour change was observed. Evaporation under vacuum merely decomposed the substance. It was not possible to obtain a pure substance but its infrared spectrum exhibited a sharp absorption at 2135 cm.$^{-1}$ and indicated

the possibility that carbon monoxide had been co-ordinated in a configuration such as has been represented.

(*Trichlorophosphine*)*carbonyldibromoplatinum*(II).—Phosphorus trichloride (0·045 g.) in carbon tetrachloride (50 ml.) was added to platinous carbonyl bromide (0·25 g.) in carbon tetrachloride (100 ml.). On evaporation to about 2 ml. and cooling overnight in dry conditions, brown-orange crystals of (*trichlorophosphine*)*carbonyldibromoplatinum*(II) were obtained (Found : Pt, 38·0. $COCl_3Br_2PPt$ requires Pt, 37·48%). Decomposition was soon apparent, even when the compound was kept over phosphoric oxide.

(*Trichlorophosphine*)*carbonyldi-iodoplatinum*(II).—Phosphorus trichloride (0·043 g.) in benzene (100 ml.) and a little acetone (20 ml.) was added to platinous carbonyl iodide (0·168 g.) in benzene (50 ml.). The colour changed immediately from orange to yellow. On evaporation a red oil was obtained which was crystallised with difficulty. The *compound* was non-conducting in M/1000-nitrobenzene solution (Found : Pt, 32·2. $COCl_3I_2PPt$ requires Pt, 31·78%).

Pyridinecarbonyldi-iodoplatinum(II).—Pyridine (0·23 ml.) was added to platinous carbonyl iodide (1·30 g.) in benzene (150 ml.). The colour of the solution changed from red to orange, and, after concentration on the water-bath, yellow-orange crystals of the *compound* were deposited; it decomposed slowly in air and rather quickly in solutions left open to the atmosphere, and it was non-conducting in M/1000-nitrobenzene solution (Found : C, 13·4; H, 1·03; I, 45·7; Pt, 35·3. $C_6H_5ONI_2Pt$ requires C, 13·0; H, 0·9; I, 45·6; Pt, 35·2%). (C and H values are high because of some decomposition before analysis.)

Dipyridinedi-iodoplatinum(II).—This compound, m. p. 270°, was obtained as bright yellow needles on addition of excess of pyridine to the preceding compound. It was described by S. G. Hedin in 1887 but the publication (*Lunds. Arskr.*) was not available. The compound did not conduct electricity in M/1000-nitrobenzene (Found : Pt, 32·3. Calc. for $C_{10}H_{10}N_2I_2Pt$: Pt, 32·3%).

Di(*methyldiphenylarsine*)*dichloroplatinum*(II).—This compound was obtained as yellow-white needles by the action of excess of methyldiphenylarsine on methyldiphenylarsine-carbonyldichloroplatinum(II); it was non-conducting in M/1000-nitrobenzene solution and was probably the *cis*-form described by Nyholm [25] (Found : Pt, 25·5. Calc. for $C_{26}H_{26}Cl_2As_2Pt$: Pt, 25·8%).

Di(*methyldiphenylarsine*)*di-iodoplatinum*(II).—This compound was similarly obtained by use of the corresponding di-iodo-analogue; [13] recrystallisation from benzene afforded yellow needles (Found : Pt, 20·8. Calc. for $C_{26}H_{26}I_2As_2Pt$: Pt, 20·8%).

Attempted Preparation of trans-*Di*(*methyldiphenylarsine*)*carbonylchloroplatinum*(II) *Chloride*.—Many attempts were made to prepare this compound by the action of molar quantities of methyldiphenylarsine on *cis*-methyldiphenylarsinecarbonyldichloroplatinum(II), and by the action of 4 moles of the arsine on one of the chloride dimer, at temperatures down to −50°. In most cases carbon monoxide was evolved and *trans*-di(methyldiphenylarsine)dichloroplatinum(II) (which isomerises to the *cis*-form [25]) was obtained. In another attempt, *trans*-di(methyldiphenylarsine)dichloroplatinum(II) (*ca.* 1·0 g.) was kept above its m. p. (200—210°) for 45 min., during which carbon monoxide was bubbled through the melt. The resulting substance was ground, and its infrared spectrum examined, a band of medium strength being observed at 2105 $cm.^{-1}$ (as opposed to the C–O frequency of *cis*-methyldiphenylarsinecarbonyldichloroplatinum(II) of 2111 $cm.^{-1}$). The conductivity of the substance in M/1000-nitrobenzene solution (*M* being assumed to be 754) was approx. 10 mhos. It was not possible to separate the compounds present. These results were interpreted as indicating the presence of some *trans*-dimethyldiphenylarsine)carbonylchloroplatinum(II) chloride in the product.

Attempted Preparation of trans-*Methyldiphenylarsinecarbonyldichloroplatinum*(II).—Methyldiphenylarsine (0·18 g.) in benzene (20 ml.) was added to pyridinium carbonyltrichloroplatinite (0·15 g.) in benzene (30 ml.) and dry acetone (20 ml.). An immediate evolution of gas occurred, and the infrared spectrum of the substance obtained on evaporation showed no carbonyl absorption.

Attempted Preparation of trans-*Methyldiphenylarsinecarbonyl-bromo- and -iodo-platinum*(II).—Methyldiphenylarsine (0·12 g.) in benzene (30 ml.) was added to pyridinium carbonyltribromoplatinite (0·17 g.) in benzene (30 ml.) and acetone (10 ml.). That the evolution of carbon monoxide was quantitative was shown by the infrared spectrum, as in the previous case. A similar reaction took place with the analogous iodine compound.

Reactions of Bidentate Ligands with the Ions $[Pt(CO)X_3]^-$.—When dipyridyl and pyridinium carbonyltri-chloro-, -bromo-, and -iodo-platinite respectively in benzene and acetone were mixed in molar proportions, precipitates were obtained which on recrystallisation from acetone yielded compounds identical (infrared spectra and molar conductivities) with those obtained from that ligand with the corresponding carbonyl halide dimers.[13]

Reactions of Hot Acetone Solutions of the Dimers $[Pt(CO)Br_2]_2$ *and* $[Pt(CO)I_2]_2$.—Molar quantities of methyldiphenylarsine reacted with acetone solutions of the platinum carbonyl bromide and iodide dimers, resulting again in the complete evolution of carbon monoxide. No carbon monoxide-containing compounds were obtained from these solutions. Less strongly double-bonding ligands such as aniline and *p*-toluidine formed the usual *trans*-derivatives under these conditions. No attempt was made to perform this reaction with the corresponding chlorine compound, as it is immediately decomposed by acetone.[23]

Potassium Carbonyltrithiocyanatoplatinum(II).—Potassium thiocyanate (3·0 g.) in 5N-hydrochloric acid (50 ml.) was added to $[Pt(CO)Cl_2]_2$ (0·5 g.) in 5N-hydrochloric acid at 0°. On cooling to −30°, the mixture solidified and a precipitate was obtained on subsequent slow warming. This was filtered off at 0°, washed, and dried (Found: Pt, 44·9. Calc. for $C_4ON_3S_3KPt$: Pt, 44·7%).

When potassium thiocyanate was added to $[Pt(CO)Cl_2]_2$ in 5N-hydrochloric acid on a water-bath the solution became orange, then red, finally depositing a red precipitate. This substance was only slightly soluble in nitrobenzene, but its conductivity in dry acetone (60 mhos) indicated the presence of more than two ions (possibly three), though such results must be regarded with caution. The compound contained carbon monoxide and may have been $(NH_4)_2[Pt(CO)(CNS)_4]$ (Found: Pt, 40·4. Calc. for $C_5H_8ON_6S_4Pt$: Pt, 39·7%).

Attempted Preparation of a Cyanide Complex.—Potassium cyanide (6 ml. of a 1% solution was added to $[Pt(CO)Cl_2]_2$ (0·5 g.) in concentrated hydrochloric acid at −40°. There was immediate evolution of carbon monoxide and it was not possible to obtain any intermediate product. The striking colour change noted by Mylius and Foerster [7] was not observed. Potassium tetracyanoplatinite was obtained from the solution.

Conductometric Titrations.—Acetone for use as solvent in these titrations was freshly distilled after being dried ($CaCl_2$) under reflux. Conductivities were measured with a dip-type cell with platinum electrodes coated with platinum-black, and with a cell constant of 1·52 (referred to potassium chloride at 20°). A "Philoscope" conductivity bridge was used. The reaction vessel was immersed in a large beaker, containing acetone–solid carbon dioxide at approximately −5°. Diarsine, phosphorus trichloride, and pyridine were added in an acetone solution of appropriate concentration from a 10 ml. burette.

Infrared measurements were carried out on paraffin mulls of the solid compounds as described in Part I,[13] except where otherwise specified.

The authors acknowledge helpful criticism from a Referee and thank Drs. F. P. Dwyer and R. L. Martin for valuable discussions on reaction mechanisms. They are also indebted to Dr. E. Challen and Mr. D. Weedon for carbon, hydrogen, and nitrogen microanalyses.

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[23] Irving and Magnusson, unpublished work.
[24] Gelman and Baumann, *Compt. rend. Acad. Sci. U.R.S.S.*, 1938, **18**, 645.
[25] Nyholm, *J.*, 1950, 843.

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388. *Reactions of the Cobaltic Ion. Part VI.*[1] *Decomposition of Hydroperoxides in Aqueous Solution and in Glacial Acetic Acid.*

By J. A. Sharp.

The kinetics of the reaction of cobaltic ion with (*a*) *tert.*-butyl hydroperoxide in dilute sulphuric acid, glacial acetic acid, and acetic–sulphuric acid mixture; and (*b*) the hydroperoxide of 2-methylbut-2-ene in dilute sulphuric acid have been measured. The reaction in all the solvents obeys a bimolecular rate relation.

$$-d[Co^{3+}]/dt = k[Co^{3+}][RO{\cdot}OH]$$

and k for *tert.*-butyl hydroperoxide was 8·52, 0·78, and 0·0255 min.$^{-1}$ for 0·09N-H_2SO_4, 87½% acetic acid–12½% 10N-sulphuric acid (v/v), and glacial acetic acid respectively. This change in reactivity of the cobalt salt is a result of complex formation in solution. The bearing of the results on the autoxidation of olefins by the cobalt salt is discussed.

The cobaltic ion interacts with the double bond of a series of unsaturated hydrocarbons

$$R^1R^2C{:}CHR^3 + Co^{3+} \longrightarrow Co^{2+} + R^1R^2\dot{C}{-}\overset{+}{C}HR^3 \quad . \quad . \quad . \quad . \quad (1)$$

[scheme (1)] forming a very reactive radical ion.[1] This radical (R) could initiate the typical autoxidation chain reaction

$$R{\cdot} + O_2 \longrightarrow RO_2{\cdot}$$

$$RO_2{\cdot} + RH \longrightarrow RO{\cdot}OH + R{\cdot}$$

where RH represents the hydrocarbon. On the other hand, the kinetic measurements of the autoxidation of some olefins [2] show that the initiating process is the reaction of the cobaltic ion with a hydroperoxide, invariably present in minute amounts in the olefin or readily formed by a thermal reaction

$$Co^{3+} + RO{\cdot}OH \longrightarrow Co^{2+} + RO_2{\cdot} + H^+ \quad . \quad . \quad . \quad . \quad . \quad (2)$$

Which of these reactions initiates the chain is determined by the relative rates of schemes (1) and (2) Part IV. We measured the rates of reaction of cobaltic ion with hydroperoxides in dilute acid and in glacial acetic acid and compared the results with measurements of the direct reaction with the olefin. The results indicate that in acetic acid the decomposition of hydroperoxide is probably the chain-initiating reaction in olefinic oxidation.

Decomposition of Hydroperoxide of 2-Methylbut-2-ene in Sulphuric Acid Solution.—A solution of the hydroperoxide of 2-methylbut-2-ene was obtained by aqueous extraction of the hydroperoxide from the olefin which had been oxidised by air for two months. The aqueous solution also contained 2-methylbut-2-ene at its saturation value. The concentration of hydroperoxide was determined by adding an excess of a solution of ferrous sulphate in dilute sulphuric acid and determining the concentration of ferric ion by its absorption at 300 mμ with the Unicam spectrophotometer. The extinction coefficient of ferric sulphate in the same media was previously determined for calibration purposes.

In a solution of excess of the hydroperoxide the rate of disappearance of cobaltic ion followed a first-order relation as shown in Fig. 1. The rate was markedly dependent on hydrogen-ion concentration, in direct contrast to the results observed with the olefin alone (Part IV). Plots of the first-order rate constant, $k_{obs.}$, against the reciprocal of the hydrogen-ion concentration for initial hydroperoxide concentrations of (1) $2{\cdot}86 \times 10^{-3}$M and (2) $0{\cdot}60 \times 10^{-3}$M are given in Fig. 2. These results show that at high hydrogen-ion concentration the hydroperoxide reaction becomes slow and of the same order as that of the direct olefin oxidation as indicated by the intercept on the ordinate. At hydrogen-ion concentrations above 0·1N the rate constant

[1] Parts IV and V, *J.*, 1957, 1854, 1866.
[2] Bawn, Pennington, and Tipper, *Discuss. Faraday Soc.*, 1951, **10**, 282; Bawn, *ibid.*, 1953, **14**, 181.

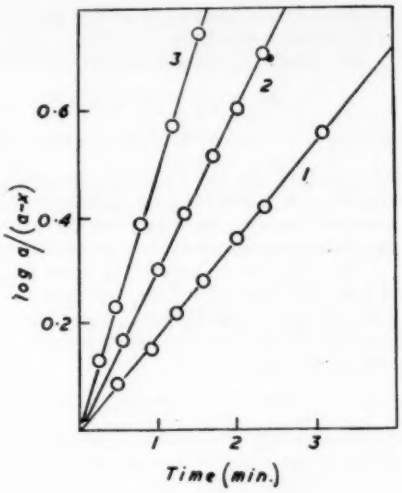


FIG. 1. *First-order plot for decomposition of the hydroperoxide of 2-methylbut-2-ene by cobaltic sulphate at 20°.*

$a = 10^{-4}$M; Hydroperoxide concn. $= 2{\cdot}86 \times 10^{3}$M. Hydrogen-ion concn.: (1) 3·30, (2) 1·67, (3) 0·67N.

FIG. 2.

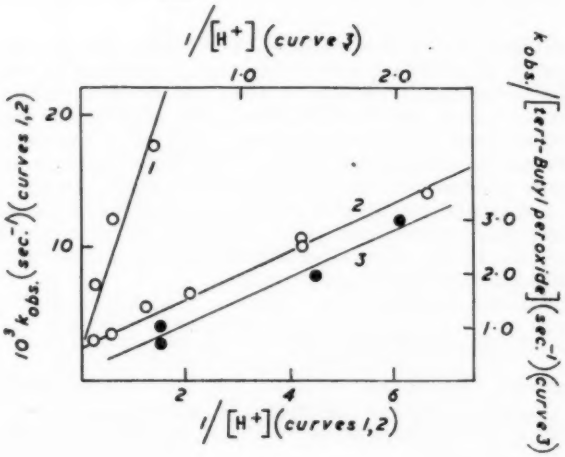
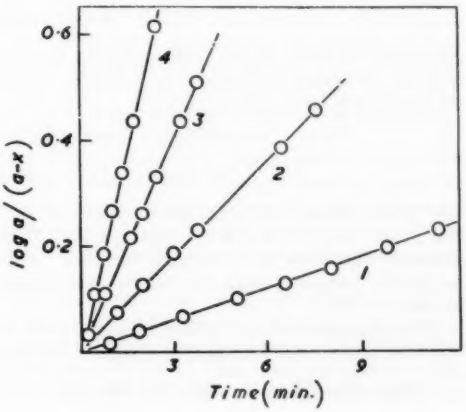


FIG. 3. *First-order plot for decomposition of* tert.*-butyl hydroperoxide at 20°.*

$a = 10^{-4}$M. Curve (1): [RO·OH] $= 0{\cdot}69 \times 10^{-3}$M; [H+] = 2·0N; Curve (2): [RO·OH] $= 2{\cdot}76 \times 10^{-3}$M; [H+] = 2·0N; Curve (3): [RO·OH] = 2·76M; [H+] = 0·67N; Curve (4): [RO·OH] $= 3{\cdot}28 \times 10^{-3}$M; [H+] = 0·48N.



k_{obs} was a linear function of $1/[H^+]$ but at lower ones this relation is modified by the occurrence of the cobaltic ion–water reaction.

The general expression for the rate of loss of cobaltic ion may be written

$$-d[Co^{3+}]/dt = k[Co^{3+}][RH] + k'[Co^{3+}][RO{\cdot}OH] + k''[Co^{3+}][RO{\cdot}OH]/[H^+]$$

or $$-d \log [Co^{3+}]/dt = k_{obs.} = k[RH] + k'[RO{\cdot}OH] + k''[RO{\cdot}OH)/[H^+]$$

At large $[H^+]$ the last term becomes negligible and the results in Fig. 2 show that under these conditions $k_{obs.}$ (for constant 2-methylbut-2-ene concentration) was not appreciably changed for a 4·8-fold increase in hydroperoxide concentration. It is evident therefore that $k' \ll k''$ and that the measured reaction is predominantly that between the cobaltic and hydroperoxide ions.

The value of k'' calculated from $dk_{obs.}/d(1/[H^+]) = k''$ for hydroperoxide concentrations of 0·60 and $2{\cdot}80 \times 10^{-3}$ are 1·65 and $8{\cdot}3 \times 10^{-3}$M respectively and for $k''/[RO{\cdot}OH]$ are 2·75 and 2·90 sec.$^{-1}$ respectively. The close agreement of these results justifies the first-order dependence of the rate on hydroperoxide concentration, and the representation of the overall rate by the equation

$$-d[Co^{3+}]/dt = k[Co^{3+}][\text{2-methylbut-2-ene}] + 2{\cdot}8[Co^{3+}][\text{hydroperoxide}]/[H^+]$$

Comparison with the results of the direct reaction with the olefin (Part IV) shows that in 0·09M-sulphuric acid at 20° the bimolecular constant for the decomposition of 2-methylbut-2-ene hydroperoxide is 15·7 times the bimolecular constant of the oxidation of 2-methylbut-2-ene by cobaltic sulphate.

Decomposition of tert.*-Butyl Hydroperoxide in Acid Solution.*—This section records preliminary measurements on the reaction of cobalt ion with *tert.*-butyl hydroperoxide in acid carried out (*a*) to determine the effect of peroxidic impurities on the rate of the direct reaction with the olefin (Part IV) and (*b*) for comparison with the rate measurement in acetic acid and mixtures of acetic acid and sulphuric acid recorded in the next section. The rate of disappearance of cobaltic sulphate in the presence of excess of *tert.*-butyl hydroperoxide was observed by a procedure similar to that used to measure the oxidation of olefins (Part IV). The rates were of the first order with respect to cobaltic-ion concentration as shown in Fig. 3, and of first order with respect to hydroperoxide concentration (Table). Under the experimental conditions the decomposition of cobaltic ion by water was negligible, and the reaction with the hydroperoxide fast compared with the direct reaction with the olefin.

A plot of the bimolecular rate constant k as given by

$$-d[Co^{3+}]/dt = k[Co^{3+}][RO{\cdot}OH]$$

against the reciprocal of the hydrogen-ion concentration was linear (Fig. 2, curve 3) and hence the reaction rate obeys the relation $-d[Co^{3+}]/dt = k'[Co^{3+}][RO{\cdot}OH]/[H^+]$ where $k' = 1{\cdot}42$ sec.$^{-1}$ at 20°. This result indicates that the rate-determining reaction is that of the cobaltic ion with the hydroperoxide ion

$$RO{\cdot}O^- + Co^{3+} \longrightarrow RO{\cdot}O{\cdot} + Co^{2+}$$

The concentration of the hydroperoxide ion is given by $[RO{\cdot}O^-] = K[RO{\cdot}OH]/[H^+]$ where K is the ionisation constant of the hydroperoxide. A similar result was observed for the reaction of formic acid with cobaltic ion: [3]

$$H{\cdot}CO_2H + Co^{3+} \longrightarrow H{\cdot}CO{\cdot}O{\cdot} + H^+ + Co^{2+} \quad . \quad . \quad . \quad . \quad . \quad \text{(i)}$$

or $$H{\cdot}CO{\cdot}O^- + Co^{3+} \longrightarrow H{\cdot}CO{\cdot}O{\cdot} + Co^{2+} \quad . \quad . \quad . \quad . \quad . \quad . \quad \text{(ii)}$$

and it was found that the rate constants of (i) and (ii) were $6{\cdot}8 \times 10^{17} \exp(-26{\cdot}9/\boldsymbol{RT})$ and $2{\cdot}0 \times 10^{18} \exp(-21{\cdot}7/\boldsymbol{RT})$ respectively. With *tert.*-butyl hydroperoxide the experimental evidence indicates that reaction between cobaltic ion and the undissociated molecule was negligible compared with that of the hydroperoxide ion over the hydrogen-ion concentration range 0·5—2·0N.

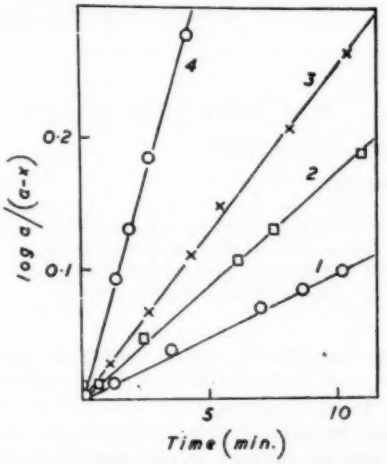
Decomposition of tert.*-Butyl Hydroperoxide in Glacial Acetic Acid and in Acetic–Sulphuric Acid Mixtures.*—On addition of a solution of 2-methylbut-2-ene in acetic acid to a solution of

[3] Bawn and White, *J.*, 1951, 331, 339, 344.

electrolytically prepared cobaltic acetate in glacial acetic acid, the absorption of the solution does not change over a period of days, showing that the olefin is not oxidised by cobaltic acetate. An identical experiment, in which cobalt acetate prepared by dissolving pure dry cobaltic sulphate in acetic acid was used, confirmed this result.

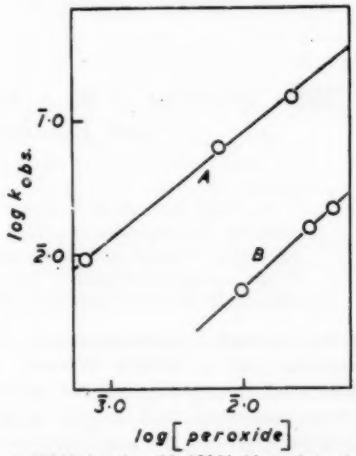
In the autoxidation of 2-methylbut-2-ene in acetic acid in the presence of cobaltic acetate, previous investigations [2] have established the formation of hydroperoxide as the initial product of the oxidation. Thus it is probable that the catalytic effect of cobaltic acetate in these systems depends on an initial reaction between cobaltic acetate and the hydroperoxide molecule formed thermally to yield a free radical which initiates a chain reaction.

FIG. 4. *First-order plots of the reaction of cobaltic ion with* tert.*-butyl hydroperoxide in sulphuric acid mixtures at* 20°.



$a = 1{\cdot}92 \times 10^{-4}$M. Curves (2) and (3), glacial acetic acid, $[RO{\cdot}OH] = 5{\cdot}0 \times 10^{-2}$M and $3{\cdot}3 \times 10^{-2}$M respectively. Curves (1) and (4), 87½% acetic acid–12½ 10N-sulphuric acid, $[RO{\cdot}OH] = 0{\cdot}066$ and 0·66M respectively.

FIG. 5.



A, 87½% Acetic acid–12½% 10N-sulphuric acid.
B, Glacial acetic acid.

In order to check this mechanism, the rate of reduction of cobaltic acetate by *tert.*-butyl hydroperoxide in glacial acetic acid was measured by observing the decrease in the absorption intensity of the cobaltic complex with the Unicam spectrophotometer as described in Part IV. The rate of this reaction was of the first order with respect to cobaltic acetate, as shown in Fig. 4.

The slope of the first-order plots was proportional to the concentration of *tert.*-butyl hydroperoxide and the plot of the logarithm of the rate constant so derived against the logarithm of the hydroperoxide concentration was linear and of slope of approximately 1·0 (Fig. 5).

The rate of reduction of cobaltic acetate in glacial acetic acid can therefore be represented by the expression $-d[Co^{3+}]/dt = k[Co^{3+}][RO{\cdot}OH]$ where $k = 0{\cdot}0225$ min.$^{-1}$ at 25°.

When cobaltic sulphate, dissolved in 87½% acetic acid–12½% 10N-sulphuric acid (v/v) was used in place of cobaltic acetate in glacial acetic acid the rate was still found to be of the first order with respect to cobaltic-ion concentration and approximately of the first order with respect to *tert.*-butyl hydroperoxide (Fig. 5), but now the value of k was increased by a factor of about 35, showing that the sulphate–acetate complex is a far stronger oxidising agent than pure cobaltic acetate.

The rate of reduction of cobaltic complex in 87½% acetic acid–12½% 10N-sulphuric acid at 25° is given by $-d[Co^{3+}]/dt = 0{\cdot}78[Co^{3+}][RO{\cdot}OH]$ min.$^{-1}$. Therefore, in dilute sulphuric acid solution in which the cobaltic ion is not highly complexed the corresponding rate of reduction is more than 100 times faster than in the dilute mixed acids (Part IV). These comparative measurements emphasise the power of complex-forming groups in defining the oxidative power of the

cobaltic ion. A full discussion of the nature of the reaction which occurred in mixed acetic and sulphuric acid mixture will be given in Part VIII.

It may be concluded that cobaltic acetate in glacial acetic acid reacts immeasurably more quickly with the hydroperoxide than with the olefin, and that the catalysing power of cobaltic acetate in the oxidation of hydrocarbons is due to its reaction with hydroperoxide, present initially as impurity and rapidly produced in small amounts by a thermal chain reaction.

tert.-Butyl hydroperoxide (10^3M)	[H^+]	$10^3k_{obs.}$ (sec.$^{-1}$)	$k_{obs.}$ [H^+]/[RO·OH] (mole l. sec.$^{-1}$)
2·76	2·0	2·16	1·65
2·76	0·70	5·18	1·32
0·69	2·00	0·75	2·16
3·28	0·48	10·1	1·54

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389. *Reactions of the Cobaltic Ion. Part VII.* The Stability and Reactivity of Cobaltic Acetate.*

By J. A. SHARP.

Cobaltic acetate in aqueous solution is rapidly reduced to the cobaltous state by the addition of dilute mineral acids. The kinetics of this process have been studied and it is concluded that the primary process is a change of the anions surrounding the cobaltic ion. Some additional properties of cobaltic acetate are summarised.

THE very powerful oxidising action of the cobalt ion towards a wide variety of organic compounds such as olefins, alcohols, aldehydes, and acids has already been reported.[1] In this work the readily isolable cobaltic sulphate which forms stable solutions in acids has been employed, and in spite of the complex features of these reactions the broad general principles of the reactivity emerged in that the primary process was an electron transfer between the cobaltic ion and the organic molecules with the formation of a free radical.

In view of the difficulties of handling cobaltic sulphate and of preparing it free from mineral acid it is preferable in kinetic studies to employ the more stable cobaltic acetate. Little is known about this substance, so a preliminary study of its preparation and properties was carried out.[2] In the present work the stability of aqueous solutions has been investigated and the kinetics of its decomposition in mineral acid measured.

Properties of Cobaltic Acetate.—Cobaltic acetate prepared by electrolytic oxidation and purified as already described [2] is stable at room temperature but decomposes at 100° with the evolution of acetic acid. It forms stable solutions in acetic acid and ethyl alcohol and the oxidising power of these solutions remains constant for several months at normal temperatures. The solutions, when heated to 70°, decompose into acetic acid and cobaltous acetate. In aqueous solution the acetate hydrolyses slowly to gelatinous cobaltic hydroxide, and thus behaves differently from other simple cobaltic salts which rapidly decompose in water. Dilute sodium hydroxide or carbonate precipitated cobaltic hydroxide but in dilute mineral acids the cobaltic acetate was reduced to the cobaltous state within a few minutes. The factors which determine this reduction have been investigated and will be described later.

As shown by Sharp and White [2] the absorption spectra of solutions at 2000—10,000 Å

* Part VI, preceding paper.

[1] Bawn and White, *J.*, 1951, 331, 339, 343; Bawn and Sharp, *J.*, 1957, 1854; Hargreaves and Sutcliffe, *Trans. Faraday Soc.*, 1955, **51**, 786.

[2] Sharp and White, *J.*, 1952, 110.

were similar for acetic acid, alcohol, and water as solvents. The presence of a small amount of cobaltous acetate in the cobaltic salt had a negligible effect on the spectra as its maximum molar extinction coefficient (at 5100 Å) was 0·02 of that of cobaltic acetate and the absorption decreased markedly on both sides of the 5100 Å peak. Measurements in these solvents over the wide concentration range $3{\cdot}0 \times 10^{-5}$—$1{\cdot}5 \times 10^{-2}$M showed that the absorption at any wavelength was directly proportional to the concentration of the cobaltic acetate in solution. This method, supplemented by other analytical procedures, was used to follow the change in cobaltic concentration in the kinetic studies reported below. Dr. Sutcliffe in this laboratory has shown that the absorption spectra of solutions of cobaltic acetate are similar to that of cobaltic sulphate and cobaltic perchlorate, indicating that the acetate is a simple cobaltic salt $Co(OAc)_3$ rather than a hexaco-ordinated complex $H_3Co(OAc)_6$. The visible maximum in absorption is at 5000 Å and the ultraviolet absorption is not as intense. In the visible region the steep increase in absorption corresponding to the electron-transfer spectrum starts at a higher wavelength with the acetate than with either the sulphate or perchlorate. In glacial acetic acid the spectrum is more intense than in water, which is in agreement with the view that the salt is ionised in water. Sharp and White [2] showed by conductivity measurements that cobaltic acetate was appreciably ionised in water whereas in glacial acetic acid the equivalent conductivity, which was independent of the age of the solution, was $3{\cdot}93 \times 10^{-3}$ mhos (mole/l.)$^{-1}$ for a solution of 0·00724N-cobaltic acetate. At this concentration the degree of ionisation is thus $4{\cdot}3 \times 10^{-3}$.

The spectrum of the cobaltic salt formed in dilute aqueous acetic acid by the oxidation of cobaltous acetate with ozone has recently been measured by Hill.[3] The spectrum is of the same type as that obtained with cobaltic acetate but the positions of the maxima obtained by Hill are displaced about 300 Å towards the ultraviolet. Hill suggests that the absorbing species was the $Co(OAc)^{2+}$ ion but no real evidence is given to substantiate this view.

The Stability of Aqueous Solutions of Cobaltic Acetate.—As already stated the addition of dilute sulphuric acid to an aqueous solution of cobaltic acetate causes complete reduction to the cobaltous state. The rate of this reaction was measured over a range of acid concentrations by following the decrease in concentration of cobaltic ion with a Unicam

TABLE 1. *Second-order decomposition of cobaltic acetate measured with Unicam spectrophotometer at* 300 mμ. *Temp.* = 17°.

$[H^+]$	$10^3[Co^{3+}]_{initial}$	$10k$ (l. mole^{-1} sec.$^{-1}$)	$\frac{10^4k[Co^{3+}]_{initial}}{[H^+]}$
0·6	2·29	4·00	15·3
0·6	1·53	7·83	20·0
0·6	0·76	14·0	17·8
1·2	0·76	26·5	16·9
1·8	0·76	33·0	14·0
0·9	0·76	20·3	17·2
1·2	1·53	13·7	17·3
Measured with Spekker spectrometer with orange filter. Temp. = 18°.			
0·385	0·541	14·50	21·0
0·154	0·72	4·22	19·7
0·77	3·56	4·40	20·4
1·54	2·12	13·00	17·9
1·54	1·22	26·00	20·6

TABLE 2. $[Co^{3+}]_{initial} = 2{\cdot}9 \times 10^{-3}$ M. Temp. = 20°. $[H^+] = 0{\cdot}30$.

$Me{\cdot}CO_2H$ (M)	$10k$ (l. mole^{-1} sec.$^{-1}$)	D_2
0·0	3·10	0·827
0·024	3·24	0·932
0·073	3·95	0·911
0·121	4·35	0·955
0·243	6·00	0·895
0·486	6·35	0·826
0·729	6·57	0·766
2·43	4·71	0·646
4·86	3·10	0·613
12·15	2·06	0·557

spectrophotometer as described in Part IV.[4] The decrease in absorption was rapid over the first few minutes and this was followed by a slower decrease at a rate which was of the

[3] Hill, *J. Amer. Chem. Soc.*, 1949, **71**, 2434.
[4] Bawn and Sharp, *J.*, 1957, 1854.

second order with respect to the change in optical density. Typical data showing the plot of the reciprocal of the optical density with time at several acid concentrations are shown in Fig. 1. Investigation of the factors determining the initial decrease showed that it was greater with high sulphuric acid concentration (Table 1); $k = d(1/[Co^{3+}])/dt$. It was also greater for larger concentrations of acetic acid added to the dilute sulphuric

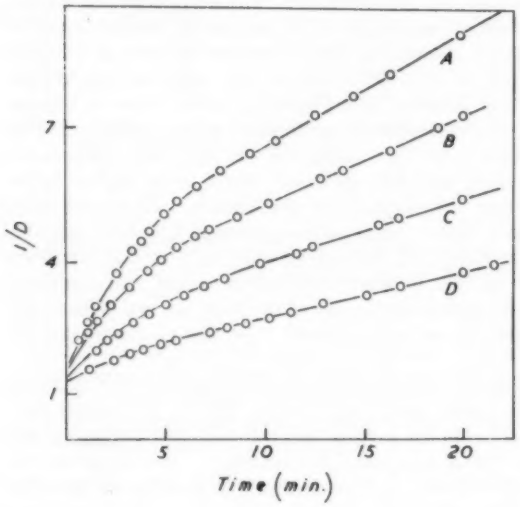


FIG. 1. *Rate of alteration of optical density D at* 3000 Å (10 *cm. cell*).

$[Co^{3+}]_{initial} = 0{\cdot}76 \times 10^{-4}$M. Hydrogen-ion concn.: *A* 1·8, *B* 1·2, *C* 0·9, *D* 0·6M.

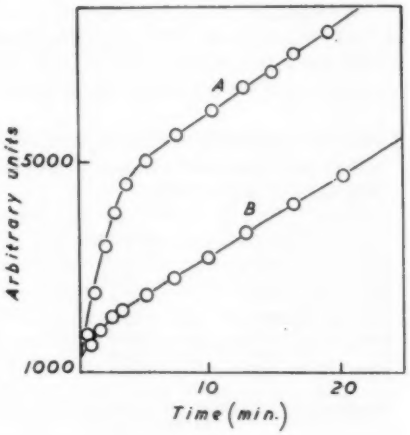


FIG. 2. *Plots of reciprocals of* (*A*) *optical density and* (*B*) *concentration against time.*

acid solution in which the cobaltic acetate was originally dissolved as shown in Table 2 (D_2 is the ratio of the optical density at the onset of the second-order rate to the initial optical density). The changes can be understood if the initial rapid decrease in absorption is associated with a change in the anions surrounding the cobaltic ion rather than the reduction to the cobaltous state, since cobaltic sulphate is known to have a lower absorption intensity than cobaltic acetate [3] and if a solution of cobaltic acetate in water has a lower absorption than a solution in acetic acid. If this suggestion is correct then the decrease in absorption with time will not parallel the change in oxidising power with time for the

same reaction. With a readily oxidisable substrate such as ferrous iron which is equally rapidly oxidised by cobaltic sulphate, acetate, or intermediate species the latter reaction will measure only the reduction of cobaltic to cobaltous independently of any change in optical absorption. These changes were investigated by observing the decrease in absorption of the solution and simultaneously the decrease in oxidising power by running small samples of the solution into excess of standard ferrous ammonium sulphate solution at fixed intervals and estimating the ferrous ion consumed by back titration with permanganate. Typical plots for a single reaction are shown in Fig. 2. The results confirm the view that the initial rapid decrease in absorption is not associated with a decomposition but with a modification of the co-ordination shell of the ion. The slower stage of the reaction obeys a second-order relation for both the decrease in oxidising power and the decrease in absorption (Fig. 2).

A study of the factor affecting the second stage of the reaction showed (*a*) that all rates were proportional to the square of the cobaltic concentration (Fig. 1); (*b*) that the rates were inversely proportional to the total cobalt ion concentration, which is equivalent to the initial cobaltic concentration (Table 1) [this surprising result in conjunction with (*a*) appears to indicate an overall first-order relationship; this order was not obeyed and all results conformed to the second-power law in cobaltic concentration]; (*c*) that the second-order rates were directly proportional to the hydrogen-ion concentration (Table 1); (*d*) that the effect of the addition of increasing amounts of acetic acid to the solution in sulphuric acid, the pH being kept constant, showed an initial increase in rate of reduction followed by a decrease in rate at higher acetic acid concentration (Table 2). The kinetic results in sulphuric acid may be summarised by the relation $-\mathrm{d}[Co^{3+}]/\mathrm{d}t = k[Co^{3+}]^2[H^+]/[Co^{3+}]_{initial}$, where $k = 1{\cdot}7 \times 10^{-3}$ l. mole^{-1} sec.$^{-1}$ at 17°. In the presence of acetic acid the rate law contains an additional multiplication term $[AcOH]^x$ where x depends on the acetic acid concentration. Although it is not yet possible to formulate a complete mechanism which accounts for the observed rate law the general picture of the reaction which has emerged is that the addition of sulphuric acid to the cobaltic acetate solution causes a rapid exchange of the anions bound to the cobalt ion. The newly formed cobaltic complex is much less stable than the acetate and the square term in $[Co^{3+}]$ indicates that reduction to Co^{2+} occurs by interaction of two Co^{3+} complexes. A similar term in the rate expression is observed in the cobaltic ion reaction with water [1] and in the decomposition of tetralin hydroperoxide by cobaltic salts.[5]

The author thanks Professor C. E. H. Bawn for his interest and advice.

Department of Inorganic and Physical Chemistry,
The University, Liverpool. [*Received, October 12th*, 1956.]

[5] Woodward and Mesrobian, *J. Amer. Chem. Soc.*, 1953, **75**, 6189.

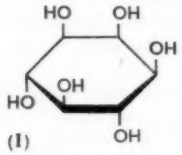
390. *Phospholipids. Part I. The Hydrolysis of Some Esters of* cyclo*Hexanediol Phosphates.*

By D. M. Brown and (Miss) H. M. Higson.

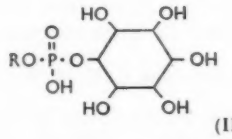
cis- and *trans*-2-Hydroxy*cyclo*hexyl phosphate and their benzyl esters are prepared. Hydrolysis of the esters by alkali or acid yields the diol phosphates and in each case proceeds more readily than that of dialkyl phosphates lacking a vicinal hydroxyl function; the evidence indicates that *cis*- and *trans*-1 : 2-*cyclo*hexylidene phosphate are intermediates in the hydrolyses. Such cyclic phosphates have been synthesised and are readily hydrolysed by acid or alkali. *cis*-1 : 3-*cyclo*Hexylidene phosphate, in contrast, is very stable. The results, together with observations already recorded, indicate phosphoryl migration during hydrolysis of the *myo*-inositol-containing phospholipids to inositol mono- or di-phosphate.

Among the phospholipids there exists a widely distributed and apparently diverse group of natural products containing *myo*inositol (I). In addition to phosphate, each individual may contain glycerol, long-chain fatty acids, sugars, and nitrogenous bases as constituent residues although, since it is not clear whether any one of these lipids has been obtained pure, contaminants may account for some of the constituents reported. Discovered first by Anderson [1] in the lipids of the tubercle bacillus, phosphoinositides have since been isolated from other bacterial, plant, and animal sources.[2] They yield *myo*-inositol monophosphate or, in the case of the brain lipid, inositol diphosphate, on hydrolysis.

Substances isolated from wheat germ,[3] liver,[4,5] heart muscle,[6] and possibly soya bean [7] appear to be relatively simple in constitution. They contain fatty acids, glycerol, inositol, and phosphate in the ratio 2 : 1 : 1 : 1 and on hydrolysis yield inositol monophosphate. The structure (II; R = diacylglycerol residue) has therefore been suggested. Others, more complex, may contain (II) as a structural unit with further substituents on the inositol fragment, for example glycosyl [8,9] or phosphorylated residues.[10]



(I)



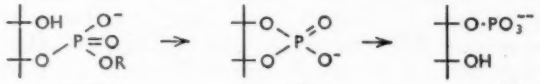
(II)

The inositol phosphates isolated after hydrolysis of phosphoinositides have not been investigated in detail and little comment seems to have been made on the possibility of phosphoryl migration on the inositol residue during hydrolysis. Thus Folch [11] has assumed that the orientation of the phosphate groups in the brain inositide is the same as that in the so-called " inositol meta-diphosphate " isolated from it on hydrolysis by mineral acid. Malkin and Poole [9] mention the possibility of phosphate migration without further comment. Hawthorne and Chargaff [10] regard phosphoryl migration as

[1] Anderson, *J. Amer. Chem. Soc.*, 1930, **52**, 1607.
[2] For refs. see Folch and LeBaron, *Canad. J. Biochem. Physiol.*, 1956, **34**, 305.
[3] Faure and Morelec-Coulon, *Compt. rend.*, 1953, **236**, 1104.
[4] McKibbin, *Fed. Proc.*, 1954, **13**, 262; *J. Biol. Chem.*, 1956, **220**, 537.
[5] Hawthorne, *Biochem. J.*, 1955, **59**, ii.
[6] Faure and Morelec-Coulon, *Compt. rend.*, 1954, **238**, 411.
[7] Okuhara and Nakayama, *J. Biol. Chem.*, 1955, **215**, 295; see however ref. 8.
[8] Hawthorne, *Biochim. Biophys. Acta*, 1955, **18**, 389.
[9] Malkin and Poole, *J.*, 1953, 3470.
[10] Hawthorne and Chargaff, *J. Biol. Chem.*, 1954, **206**, 27.
[11] Folch, *J. Biol. Chem.*, 1949, **177**, 505.

unlikely on the grounds that the oxygen–oxygen distances in polyhydroxy*cyclo*hexane systems are too great to allow of its occurrence. This is, however, unjustified, in view of the preparation of *iso*propylidene [12] and cyclic sulphite [13] derivatives of both *cis*- and *trans-cyclo*hexane-1 : 2-diol. It seemed to us that clarification of this point was essential before any rational approach could be made, based on hydrolytic evidence, to the structures of the intact phosphoinositides.

Migration of phosphate was first recognised during hydrolysis of alkyl esters of glycerol phosphate, by Bailly and Gaumé,[14] and later in phospholipids of lecithin and kephalin type by Baer and Kates [15] who discussed a mechanism for the process. The ribonucleic acids were then shown [16] to contain analogous systems and studies of the hydrolysis of alkyl esters of the 2′- and 3′-monoribonucleotides (partial formula III; R = alkyl) have permitted a clearer view of the hydrolytic process.[17,18] This, briefly, is considered to proceed, in the case of alkaline hydrolysis, by attack of the neighbouring hydroxyl group



(III) (IV) (V)

on phosphorus with expulsion of RO^-, to give the cyclic diester (IV) which then breaks down to the two isomeric monoesters (V). Participation by the vicinal function results in (a) much greater lability of the system by comparison with normal dialkyl phosphates which are extremely stable,[19] and (b) retention of the phosphate group on the hydroxyalkyl residue, that is, with no significant production of $RO{\cdot}PO_3H_2$ from (III).[20] Acid hydrolysis, likewise, proceeds *via* the intermediate cyclic phosphate (IV) and moreover migration of the alkylphosphoryl group to the vicinal position can also occur without loss of the R group.[18]

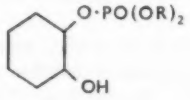
Because of the complexity of the inositol phosphate derivatives it was decided to study, first, the chemistry of their simple analogues, the hydroxy*cyclo*hexyl phosphates and their esters. Dibenzyl 2-hydroxy*cyclo*hexyl phosphate (VI; $R = CH_2Ph$), evidently the *trans*-isomer from its mode of formation from *cyclo*hexene oxide and dibenzyl phosphate, was converted by debenzylation with 4-methylmorpholine into *trans*-2-hydroxy*cyclo*hexyl benzyl phosphate [21] (VII; $R = CH_2Ph$), which on hydrogenolysis afforded *trans*-2-hydroxy*cyclo*hexyl dihydrogen phosphate (VIII).

For the preparation of members of the *cis*-series, *cis-cyclo*hexane-1 : 2-diol was treated with dibenzyl phosphorochloridate. The crystalline, but unstable *cis*-(dibenzyl phosphate) (VI) obtained could be debenzylated with lithium chloride or by partial hydrogenolysis to the monobenzyl ester (VII), whence further hydrogenolysis afforded *cis*-2-hydroxy*cyclo*hexyl dihydrogen phosphate (VIII). The last substance was more conveniently prepared by direct phosphorylation of *cis-cyclo*hexane-1 : 2-diol with phosphoryl chloride.

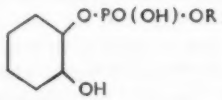
The cyclic *cis*- and *trans*-1 : 2-*cyclo*hexylidene phosphates (IX) were also prepared since they were considered to be possible intermediates in the hydrolysis of the *cis*- and the *trans*-monobenzyl ester (VII). *cis*-2-Hydroxy*cyclo*hexyl dihydrogen phosphate (VIII), when treated with trifluoroacetic anhydride,[22] was about half converted into another

[12] Christian, *Canad. J. Chem.*, 1951, **29**, 911.
[13] Price and Berti, *J. Amer. Chem. Soc.*, 1954, **76**, 1211.
[14] Bailly and Gaumé, *Bull. Soc. chim. France*, 1935, **2**, 354.
[15] Baer and Kates, *J. Biol. Chem.*, 1948, **175**, 79; 1950, **185**, 615.
[16] Brown and Todd, *J.*, 1952, 44, 52.
[17] *Idem*, *Ann. Rev. Biochem.*, 1955, **24**, 311.
[18] Brown, Magrath, Neilson, and Todd, *Nature*, 1956, **177**, 1124.
[19] Plimmer and Burch, *J.*, 1929, 279.
[20] Cf. however, Fleury, Lecocq, and le Dizet, *Compt. rend.*, 1956, **242**, 420.
[21] Baddiley, Clark, Michalski, and Todd, *J.*, 1949, 818.
[22] Brown, Magrath, and Todd, *J.*, 1952, 2708.

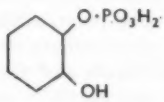
substance running faster on chromatograms. The same substance was obtained in high yield by the action of di*cyclo*hexylcarbodi-imide on the acid (VIII) in dimethylformamide.[23,24] Both reagents have been used previously for the preparation of cyclic esters in the ribonucleotide series. Applied to the *trans*-diol phosphate the latter method afforded a



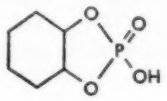
(VI)



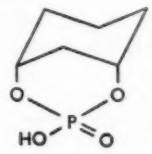
(VII)



(VIII)



(IX)



(X)

substance with very similar chromatographic characteristics. Both the *cis*- and the *trans*-derivative formed a crystalline *cyclo*hexylamine salt and on electrometric titration showed no buffering action in the pH range 5—8 associated with secondary phosphoryl dissociation. The easy hydrolysis of the substances both by acid and base, characteristic of other 5-membered cyclic phosphates,[22] together with the other evidence leads us to formulate them as the *cis*- and *trans*-isomers of the cyclic compound (IX), rather than as pyrophosphates which can arise when the carbodi-imide reagent is applied to alkyl phosphates lacking the vicinal hydroxyl function.[25]

Some phosphorylated derivatives of the *cyclo*hexane-1 : 3-diols have been prepared and their hydrolysis studied. When *cis-cyclo*hexane-1 : 3-diol was treated with dibenzyl phosphorochloridate a mixture of mono- and di-phosphorylated materials was obtained. These could not be separated nor was it possible to purify the partially debenzylated products. Complete hydrogenolysis permitted the isolation of the crystalline *cyclo*hexylamine salt of *cis*-1 : 3-*cyclo*hexylidene bisphosphate. The monophosphate, present in the mother-liquors was obtained chromatographically pure but in quantity insufficient for characterisation. *trans*-3-Hydroxy*cyclo*hexyl dihydrogen phosphate, however, was obtained by phosphorylation of *trans*-3-benzoyloxy*cyclo*hexanol followed by removal of protecting groups.

Phosphorylation of the *cis*-1 : 3-diol with phosphoryl chloride gave in high yield the *cis*-1 : 3-*cyclo*hexylidene phosphate.[26] This cyclic phosphate was extremely stable;[27] it was unaffected by 30% aqueous sodium hydroxide at 100° and was only slowly degraded, with formation of phosphoric acid, by 3N-hydrochloric acid at this temperature. It formed a crystalline methyl ester of considerable stability which with N-hydrochloric acid reverted to the cyclic phosphate (X) only, but with N-alkali yielded an additional substance stable to more prolonged treatment. This product which could not be obtained pure was almost certainly *cis*-3-hydroxy*cyclo*hexyl methyl hydrogen phosphate. Its high stability together with that of the 1 : 3-cyclic phosphate (X) is a strong indication that no participation by a *cis*-3-hydroxyl group is effective in the hydrolysis of *cyclo*hexyl alkyl phosphates. Since cyclic ester formation requires a 1 : 3-diaxial conformation it is even less likely to occur in the *myo*inositol (I) series where five oxygen atoms would then require to be axially disposed.

[23] Brown, unpublished results, quoted by Khorana (*Chem. Rev.*, 1953, **53**, 145).
[24] Dekker and Khorana, *J. Amer. Chem. Soc.*, 1954, **76**, 3522.
[25] Khorana and Todd, *J.*, 1953, 2259.
[26] Cf. Stetter and Steinacker, *Chem. Ber.*, 1952, **85**, 451.
[27] Cf. Baddiley, Buchanan, and Szabo, *J.*, 1954, 3826.

The hydrolysis of the *cyclo*hexane-1 : 2-diol phosphate derivatives was studied in more detail. Both *cis*- and *trans*-1 : 2-*cyclo*hexylidene phosphate (IX) underwent complete hydrolysis to the diol phosphate in less than 18 hr. in N-acid or -alkali at room temperature and in less than 10 min. at 100°. The rate in base for the *trans*-isomer was about twice that for the *cis*-isomer, consistently with the greater strain to be expected in a *trans*-fused 5 : 6-bicyclic system. The *cis*- and the *trans*-2-hydroxy*cyclo*hexyl benzyl phosphate (VII) were more stable than the cyclic phosphates, as expected. Thus the *trans*-isomer was recovered unchanged after two days at room temperature in N-sodium hydroxide, although the *cis*-isomer had undergone partial hydrolysis. At 100° the *cis* ester was half-hydrolysed in about 1 hr. and was completely converted in 5 hr. into a product which was isolated and characterised as *cis*-2-hydroxy*cyclo*hexyl phosphate. The *trans*-ester likewise yielded only the *trans*-2-hydroxy*cyclo*hexyl phosphate on complete hydrolysis; in neither case was a detectable amount of benzyl phosphate produced. By contrast, neither dibenzyl phosphate nor di*cyclo*hexyl phosphate was affected by N-alkali at 100° during 7 hr.

The monobenzyl esters (VII) were also hydrolysed by acid with loss of the benzyl group, the rates again being in the order *cis*- greater than *trans*-isomer; N-acid led to complete hydrolysis of the former in 20 min. whereas 2 hr. were required for the *trans*-isomer. These results are more equivocal since benzyl phosphates are known [28] to be more susceptible than other alkyl phosphates to acid hydrolysis but the large difference in rates between the *cis*- and the *trans*-isomer does indicate that the vicinal function is involved.

Taken together, these experiments strongly suggest that the hydrolysis of the monobenzyl ester of both *cis*- and *trans*-2-hydroxy*cyclo*hexyl phosphate (VII) occurs by the mechanism, discussed above, which involves the corresponding 1 : 2-*cyclo*hexylidene phosphate (IX). Alkaline hydrolysis proceeds much faster than that of normal dialkyl phosphates and only in the direction of formation of the diol phosphate (VIII). In addition the greater rate observed in the *cis*- than in the *trans*-series can be accommodated in terms of deformational strain in the *cyclo*hexane ring due to formation of the bicyclic intermediate.[29,30] The ready synthesis of the cyclic esters (IX) is also an argument in favour of the proposed hydrolytic mechanism. It is to be noted, however, that the benzyl esters (VII) are much more stable than their nucleotide counterparts (III), but this is to be expected since the stereochemistry associated with the ribofuranose residue of the latter is much more favourable to participation of the vicinal group in the ester hydrolysis.

Further experiments with glycerol esters and more fully hydroxylated *cyclo*hexyl phosphates are in progress, but the present results indicate that phosphate migration, in the absence of evidence to the contrary, must be expected to occur during hydrolysis of phosphoinositides based on (II). Moreover, during acid hydrolysis, a method hitherto used extensively in degradative work in this field, the *myo*inositol phosphate produced is probably subject to further acid-catalysed phosphate migration. Relevant to this is the recent observation [31] that such migration does occur in the case of the 3-phosphate of shikimic acid (a trihydroxy*cyclo*hexenecarboxylic acid).

Experimental

Paper Chromatography of Some cyclo*Hexyl Phosphates.*—Paper chromatography was used throughout for identification and as a criterion of purity of products. Authentic specimens were run concurrently, where possible, and spots were detected with a phosphate spray reagent. The Table contains the R_P values recorded for the substances studied; Whatman No. 1 paper and two solvent systems were used, namely, (A) propan-2-ol–water–ammonia (*d* 0·880) (7 : 2 : 1 v/v) and (B) butan-1-ol–acetic acid–water (6 : 2 : 3 v/v). No significant differences between the R_P values of *cis*- and *trans*-isomers was noted.

[28] Kumamoto and Westheimer, *J. Amer. Chem. Soc.*, 1955, **77**, 2515.
[29] Angyal and Macdonald, *J.*, 1952, 686.
[30] Eliel and Pillar, *J. Amer. Chem. Soc.*, 1955, **77**, 3600.
[31] Weiss and Mingioli, *ibid.*, 1956, **78**, 2894.

Substance	R_F values in solvent A	B
Dibenzyl 2-hydroxy*cyclo*hexyl phosphate	0·90	0·95
Benzyl 2-hydroxy*cyclo*hexyl hydrogen phosphate	0·75	0·81
2-Hydroxy*cyclo*hexyl dihydrogen phosphate	0·33	0·45
1 : 2-*cyclo*Hexylidene hydrogen phosphate	0·60	0·70
Benzyl dihydrogen phosphate	0·40	0·50
trans-3-Hydroxy*cyclo*hexyl dihydrogen phosphate	0·20	0·14
1 : 3-*cyclo*Hexylidene hydrogen phosphate	0·50	0·50
1 : 3-*cyclo*Hexylidene methyl phosphate	0·82	0·85
cis-1 : 3-*cyclo*Hexylidene bis(dihydrogen phosphate)	0·05	—

trans-2-*Hydroxy*cyclo*hexyl Dihydrogen Phosphate.*—*cyclo*Hexylammonium *trans*-2-hydroxy-*cyclo*hexyl benzyl phosphate [21] (1·03 g.) was hydrogenolysed at room temperature and pressure in ethanol (25 c.c.) over 5% palladised charcoal. After 9 hr. uptake of hydrogen was complete and the catalyst was removed by filtration. Evaporation of the solvent gave cyclo*hexyl-ammonium* trans-2-*hydroxy*cyclo*hexyl hydrogen phosphate* (0·884 g.) which formed colourless needles (from ethanol), m. p. 208—211°, softening at 180° (Found, in material dried at 80°/0·5 mm. : C, 48·8; H, 9·0. $C_{12}H_{26}O_5NP$ requires C, 48·8; H, 8·9%).

A solution of the above salt was percolated through a column of Dowex-50 (H form). Percolate and washings were evaporated to dryness; the residue crystallised from dioxan. trans-2-*Hydroxy*cyclo*hexyl dihydrogen phosphate* formed colourless needles, m. p. 164—168° (Found, in material dried at 100°/0·5 mm. : C, 36·2; H, 6·3. $C_6H_{13}O_5P$ requires C, 36·7; H, 6·6%).

Dibenzyl cis-2-*Hydroxy*cyclo*hexyl Phosphate.*—*cis-cyclo*Hexane-1 : 2-diol (4·05 g.), dried over phosphoric oxide at 0·5 mm., was dissolved in dry pyridine (10 c.c.), and the solution cooled at −20°. Dibenzyl phosphorochloridate [32] [from dibenzyl phosphite (5·1 g.)] in carbon tetrachloride was added dropwise with rigid exclusion of moisture during 0·5 hr. After being kept at −20° to −15° for 3 hr. and at 0° overnight the solution was washed with dilute sodium hydrogen carbonate solution, twice with potassium hydrogen sulphate solution, and then with water. After being dried (Na_2SO_4), the solution was evaporated at 35°/12 mm., finally with additions of ethanol to remove pyridine. The crude product (5·02 g.; 62%) was crystallised from light petroleum (b. p. 60—80°) and gave *dibenzyl* cis-2-*hydroxy*cyclo*hexyl phosphate* in needles, m. p. 64—67° (Found, in material dried at 30°/0·2 mm. for 48 hr. : C, 62·8; H, 6·7. $C_{20}H_{25}O_5P$ requires C, 63·8; H, 6·9%). Three other apparently similar preparations gave only yellow oils.

The compound and the corresponding *trans*-isomer [21] were converted within 10 min. into the monobenzyl ester when heated at 100° in N-sodium hydroxide; no dibenzyl phosphate was formed.

Benzyl cis-2-*Hydroxy*cyclo*hexyl Hydrogen Phosphate.*—To the above dibenzyl phosphate (0·49 g.) in redistilled ethyl cellosolve (15 c.c.), freshly fused lithium chloride (0·5 g.) was added and the solution then heated on the water-bath for 2 hr. To the cooled solution N-sodium hydroxide (30 c.c.) was added and unchanged starting material extracted with ether. The aqueous layer was acidified with concentrated hydrochloric acid and extracted with chloroform. The chloroform solution was dried (Na_2SO_4) and evaporated and the residual, oily benzyl *cis*-2-hydroxy*cyclo*hexyl hydrogen phosphate converted into its cyclo*hexylamine* salt by addition of *cyclo*hexylamine to its aqueous solution, to pH 10, and then evaporation to dryness. It crystallised from ethanol–ethyl acetate in needles, m. p. 187—193° (0·19 g.) (Found : C, 59·4; H, 8·4; N, 3·7. $C_{19}H_{32}O_5NP$ requires C, 59·2; H, 8·3; N, 3·6%).

The same monobenzyl phosphate was obtained as its *cyclo*hexylamine salt (0·91 g.) after (slow) hydrogenolysis of a non-crystalline sample of the above dibenzyl phosphate (1·0 g.) over palladium–charcoal.

cis-2-*Hydroxy*cyclo*hexyl Dihydrogen Phosphate.*—(*a*) The above crystalline dibenzyl ester (0·43 g.) was hydrogenated smoothly over 10% palladium–charcoal, in 95% ethanol (20 c.c.). Filtration and then evaporation gave the product as a colourless glass. The cyclo*hexylamine hydrogen phosphate* formed needles (0·23 g.) (from ethanol), m. p. 192—204° (Found, in material dried at 100°/0·5 mm. : C, 48·8; H, 8·7; N, 4·7. $C_{12}H_{26}O_5NP$ requires C, 48·5; H, 8·8; N, 5·0%).

The *cyclo*hexylamine salt (0·32 g.) was converted into the *disilver salt* by treating it in hot

[32] Atherton, Openshaw, and Todd, *J.*, 1945, 382.

water (10 c.c.) with excess of silver nitrate solution. A white granular precipitate was formed, which was collected after cooling to 0° in the dark. The amorphous product (0·35 g.) was light sensitive (Found, in material dried at 100°/0·5 mm. for 2 hr.: C, 17·8; H, 2·9; P, 7·8. $C_6H_{11}O_5Ag_2P$ requires C, 17·6; H, 2·7; P, 7·6%). Attempts to prepare the monosilver salt by using 1 mol. of silver nitrate yielded only the disilver salt.

(*b*) Pure phosphoryl chloride (0·5 c.c.) was added to dry pyridine (10 c.c.), and 8 c.c. of this solution were added dropwise with shaking to a solution of *cis-cyclo*hexane-1 : 2-diol (0·5 g.) in pyridine (5 c.c.), cooled in ice. After being set aside overnight at 0°, precipitated pyridine hydrochloride was filtered off and the pyridine removed *in vacuo*. The residue was dissolved in water, and barium hydroxide solution added to pH 10, then excess of reagent neutralised with carbon dioxide. After filtration from barium phosphate, the solution was passed through a column of Dowex-50 (H form) resin, and the acidic percolate and washings were combined and evaporated, finally at 0·5 mm. over potassium hydroxide. The crystalline residue (0·45 g.) of cis-2-*hydroxy*cyclo*hexyl dihydrogen phosphate* recrystallised from acetone as needles, m. p. 134—135° (Found, in material dried at 80°/0·5 mm.: C, 36·8; H, 6·7. $C_6H_{13}O_5P$ requires C, 36·7; H, 6·6%).

Paper chromatography of the reaction mixture showed that the 1 : 2-cyclic phosphate was the main product initially, and that this was hydrolysed during working up.

cis-1 : 2-cyclo*Hexylidene Hydrogen Phosphate*.—(*a*) Dry *cyclo*hexylammonium *cis*-2-hydroxy-*cyclo*hexyl hydrogen phosphate (115 mg.), dissolved in trifluoroacetic anhydride (5 c.c.), was set aside for 2 days with rigid exclusion of moisture. Evaporation *in vacuo* at 35° left a colourless oil. Paper chromatography in the propan-2-ol–ammonia–water solvent showed that the product was present to the extent of 50% and had a higher R_P value (0·65) than the starting material (0·33). The oil was dissolved in 3% aqueous ammonia, and sufficient propan-2-ol added to give a clear solution. This was applied to a sheet of washed seed-testing paper at the origin as a band and then chromatographed with the propan-2-ol–ammonia–water system. The product was clearly separated from starting material, and the appropriate section of the paper was cut out, eluted with water (2 × 5 c.c.), 1 : 1 aqueous ethanol (5 c.c.), and ethanol (5 c.c.). The combined eluates were filtered and evaporated *in vacuo*, and contaminating ammonium trifluoroacetate removed by microsublimation at 75°/0·5 mm. for 2 days, leaving *ammonium* cis-1 : 2-cyclo*hexylidene phosphate* (Found: C, 36·2; H, 7·2; N, 7·0. $C_6H_{14}O_4NP$ requires C, 36·9; H, 7·2; N, 7·2%).

(*b*) *cis*-2-Hydroxy*cyclo*hexyl dihydrogen phosphate prepared by hydrogenation of its dibenzyl ester (345 mg.) was dried at room temperature and 1 mm. over phosphoric oxide for 48 hr. and then dissolved in pure dry dimethylformamide (5 c.c.). Di*cyclo*hexylcarbodi-imide (217 mg.) in dimethylformamide (5 c.c.) was added slowly with shaking and the whole set aside for 2 days. *NN'*-Di*cyclo*hexylurea was filtered off and the filtrate was evaporated *in vacuo*. The residue was extracted with water, and the solution brought to pH 10 with *cyclo*hexylamine. Evaporation gave the crystalline cyclo*hexylamine salt* (91 mg., 75%), m. p. 182—188° (Found: C, 51·0; H, 8·4; N, 5·3. $C_{12}H_{24}O_4NP$ requires C, 52·0; H, 8·7; N, 5·1%).

Electrometric titration showed that no group in the molecule was titrated at pH 5—8.

trans-1 : 2-cyclo*Hexylidene Hydrogen Phosphate*.—Preparation (*b*), above, was repeated from, as starting material, *trans*-2-hydroxy*cyclo*hexyl dihydrogen phosphate (120 mg.), prepared by passing its *cyclo*hexylamine salt through a short column of Dowex-50 (H form) resin and evaporating the washings to dryness. cyclo*Hexylammonium* cis-1 : 2-cyclo*hexylidene phosphate* (89 mg.) was obtained after two crystallisations from alcohol–ether. The salt did not melt sharply, but was chromatographically homogeneous (Found, in material dried at 80°/0·5 mm.: C, 51·4; H, 8·9; N, 5·2. $C_{12}H_{24}O_4NP$ requires C, 52·0; H, 8·7; N, 5·05%). Electrometric titration demonstrated the absence of secondary phosphoryl dissociation.

cis-1 : 3-cyclo*Hexylidene Bis*(*dihydrogen Phosphate*).—*cis-cyclo*Hexane-1 : 3-diol [23] (5·0 g.) in pyridine was treated in the usual way with dibenzyl phosphorochloridate (from 11·5 g. of dibenzyl phosphite) in carbon tetrachloride. A yellow oil (12·34 g.) was obtained. The oil (1·8 g.) was hydrogenated in ethanol over 10% palladium–charcoal. After filtration and evaporation *in vacuo*, the residual oil was dissolved in water and brought to pH 10 with barium hydroxide, and excess of barium removed by carbon dioxide. After filtration, evaporation gave a colourless residue which was dissolved in the minimum of cold water and the solution filtered. On warming, the solution deposited microcrystalline *dibarium* cis-1 : 3-cyclo*hexylidene bisphosphate* (0·11 g.). For analysis two further recrystallisations were carried out (Found, in

material dried at 50°/0·5 mm.: C, 11·2; H, 3·2; P, 9·6. $C_6H_{10}O_8P_2Ba_2,4H_2O$ requires C, 11·4; H, 2·9; P, 9·9%).

The barium salt was converted into the free acid, obtained as an oil, by treatment with Dowex-50 (H form), and then into the *di*(cyclo*hexylamine*) *salt* which crystallised from aqueous acetone and had m. p. 230—245° with darkening (Found: C, 45·4; H, 8·3; N, 6·3. $C_{18}H_{40}O_8P_2N_2$ requires C, 45·6; H, 8·5; N, 5·9%).

The mother-liquors from the crystallisation of the above barium salt contained another material, faster running on chromatograms, which was evidently the *cyclo*hexane-1 : 3-diol dihydrogen monophosphate. It was separated from residual diphosphate by chromatography on a cellulose column with the propan-2-ol–ammonia solvent. Although chromatographically pure the ammonium salt from the column gave no consistent analyses and there was insufficient material for further purification.

Experiments with *trans-cyclo*hexane-1 : 3-diol showed that analogous mono- and diphosphates were formed but these could not be obtained analytically pure.

cis-1 : 3-cyclo*Hexylidene Hydrogen Phosphate*.—Pure phosphoryl chloride (1·0 c.c.) was dissolved in dry pyridine (9 c.c.). 3·9 c.c. of this solution were added dropwise with shaking to an ice-cold solution of *cis-cyclo*hexane-1 : 3-diol (0·465 g.) in pyridine. The solution, protected from moisture, was set aside overnight at room temperature and then pyridine hydrochloride was filtered off. The solution was poured into water, solvents were removed *in vacuo*, and inorganic phosphate was removed as the barium salt. The solution was freed from barium ions by means of Dowex-50 (H form) and then evaporated to dryness, finally over potassium hydroxide at 0·5 mm. to remove hydrochloric acid. cis-1 : 3-cyclo*Hexylidene hydrogen phosphate* (0·645 g.) remained as a crystalline residue. A sample was purified by crystallisation twice from water and had m. p. 170—172° (Found, in material dried at 100°/0·5 mm.: C, 40·4; H, 6·3. $C_6H_{11}O_4P$ requires C, 40·3; H, 6·2%).

The cyclo*hexylamine salt* crystallised from aqueous acetone (Found: C, 51·8; H, 8·45; N, 5·2. $C_{12}H_{24}O_4NP$ requires C, 52·0; H, 8·45; N, 5·0%).

Electrometric titration demonstrated the absence of buffering by the hydrogen phosphate in the pH range 5—8. The substance, as judged by paper chromatography, was stable to 30% sodium hydroxide solution at 100° but was slowly hydrolysed by 3N-hydrochloric acid at 100° with liberation of inorganic phosphate.

cis-1 : 3-cyclo*Hexylidene Methyl Phosphate*.—The above acid (74 mg.), in methanol (5 c.c.), was treated in the cold with ethereal diazomethane until a permanent yellow colour remained. After 1 hr. solvents were removed at 35° and the residue was crystallised from light petroleum (b. p. 40—60°). The *methyl ester* formed rosettes of needles (50 mg.), m. p. 120—127° (Found: C, 43·7; H, 6·5. $C_7H_{13}O_4P$ requires C, 43·7; H, 6·8%).

The ester was hydrolysed by aqueous-methanolic N-hydrochloric acid at 100° in 1 hr. to 1 : 3-*cyclo*hexylidene phosphate. With N-sodium hydroxide it formed the cyclic phosphate (1 part) and another compound (2 parts), probably *cis*-3-hydroxy*cyclo*hexyl methyl hydrogen phosphate, which travelled slightly faster on chromatograms and was stable to further treatment with alkali.

trans-3-*Hydroxy*cyclo*hexyl Dihydrogen Phosphate*.—*trans-cyclo*Hexane-1 : 3-diol monobenzoate [33] (4·0 g.) was phosphorylated in the usual way with dibenzyl phosphorochloridate (1 mol.). The neutral product was isolated as a yellow oil (4·5 g.), presumably crude 3-benzoyloxy*cyclo*hexyl dibenzyl phosphate. It (1·0 g.) was hydrogenolysed in ethanol (50 c.c.) over palladised charcoal. Removal of catalyst and solvent left an oil, which had R_P 0·30 in solvent system A (R_P of the dibenzyl phosphate 0·94), presumably 3-benzoyloxy*cyclo*hexyl dihydrogen phosphate. Removal of the benzoyl group was effected by heating the oil in 0·5N-sodium hydroxide for 1·5 hr. under reflux. After cooling, the solution was stirred with excess of Dowex-50 (H form). Benzoic acid was removed by ether-extraction and the aqueous layer was neutralised with *cyclo*hexylamine. The solid salt was triturated with ethanol. An insoluble residue of *cyclo*hexylamine phosphate was removed and di*cyclo*hexylamine *trans*-3-hydroxy*cyclo*hexyl phosphate separated from the filtrate on concentration. It formed needles of the *dihydrate*, m. p. 200—203° (from ethanol), R_P (in solvent A) 0·19 (Found, in material dried at 80°/0·5 mm.: C, 50·6; H, 9·9; N, 6·5. $C_6H_{13}O_5P,2C_6H_{13}N,2H_2O$ requires C, 50·3; H, 10·0; N, 6·5%).

When the above crude benzoyloxy*cyclo*hexyl dibenzyl phosphate was hydrolysed by 5%

[33] Clarke and Owen, *J.*, 1950, 2103.

aqueous-alcoholic sodium hydroxide at 100° for 1·5 hr., it gave rise to a product with R_P 0·83 in solvent A, which was stable to further alkali treatment. The substance, presumably *trans*-3-hydroxy*cyclo*hexyl benzyl hydrogen phosphate, could not however be obtained pure.

Hydrolysis of Some cyclo*Hexyl Phosphate Esters.*—(*a*) trans-2-*Hydroxy*cyclo*hexyl benzyl hydrogen phosphate.* The *cyclo*hexylammonium salt [20] (155 mg.) was heated in N-sodium hydroxide (10 c.c.) under reflux for 25 hr. Cations were removed by treatment with Dowex-50 resin (H form), and the solution was then taken to dryness. The residue was dissolved in ethanol, and *trans*-2-hydroxy*cyclo*hexyl dihydrogen phosphate was isolated as its *cyclo*hexylamine salt (102 mg.), identified by comparison of its infrared spectrum and m. p. with that of an authentic sample.

(*b*) cis-2-*Hydroxy*cyclo*hexyl benzyl hydrogen phosphate.* The *cyclo*hexylamine salt (55 mg.) was treated as above for the *trans*-isomer. The product, isolated as its *cyclo*hexylamine salt, was identified as *cis*-2-hydroxy*cyclo*hexyl dihydrogen phosphate, as above.

A chromatographic study of the hydrolysis of the above compounds showed that for the *cis*-isomer in N-sodium hydroxide at 100° half-hydrolysis occupied about 1 hr., reaction being complete in <5 hr. The *trans*-isomer was only about half-hydrolysed in 2·25 hr. With N-hydrochloric acid at 100° hydrolysis of the *cis*-isomer was complete in 20 min., but 2 hr. were required for the *trans*-isomer. No benzyl phosphate was produced under any of these conditions. A more exact study of hydrolysis rates of these and other related phosphate esters is in progress.

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391. *The Ultraviolet Absorption Spectra of Nitro-substituted Aromatic Carbonyl Compounds.*

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The ultraviolet absorption spectra of mononitro-substituted benzaldehydes, acetophenones, and *trans*-chalcones, and of certain dinitrochalcones, are reported. *ortho*-Substituents show steric effects as described by Braude,[1] and mononitrochalcones show electronic substituent effects consistent with the findings of Black and Lutz.[2] There are indications of a specific chromophoric effect from *m*- and *p*-nitrobenzoyl groupings.

o-, *m*-, and *p*-NITRO-BENZALDEHYDE and -acetophenones were obtained in order to prepare the nitro-chalcones which were required for a kinetic study (see following paper). The ultraviolet spectra of all these compounds were measured in ethyl alcohol to establish an analytical method for the kinetic work. A separate treatment of the various correlated features evident in the absorptions was considered desirable.

Benzaldehyde and Acetophenones.—The spectra of these are in Table 1. The values for bands 2 and 3 agree with those reported by Grammaticakis [3] (who did not include the low-wavelength absorption). There was, however, a greater discrepancy than expected in the values for *m*-nitro-benzaldehyde and -acetophenone and these compounds were purified with particular care before the final values were accepted. The accuracy of the values for band 1 is probably lower than of the others owing to the light-scattering defect shown by spectrophotometers at their lower range limit (see Bladon *et al.*[4]). We have checked these maxima on two instruments of different manufacture and find concordant results; from this and other considerations we believe them to be real and not " false."

The weak bands shown by the unsubstituted compounds at 330 mμ were not sought in

[1] Braude and Sondheimer, *J.*, 1955, 3754.
[2] Black and Lutz, *J. Amer. Chem. Soc.*, 1955, **77**, 5134.
[3] Grammaticakis, *Bull. Soc. chim. France*, 1953, 821, 856.
[4] Bladon, Henbest, and Wood, *J.*, 1952, 2737.

the nitro-derivatives. No significance is attached to the frequent failure of the latter to show band 3 since this may well be overwhelmed by the broad maximum of band 2.

We identify the second bands of Table 1 with Braude's *K*-bands [5] since they correspond with the similarly placed bands both of unsubstituted compounds and of nitrobenzene ($\lambda_{max.}$ 252 mμ; ε 10,000). Bowden and Braude [6] associate such bands with transitions to a dipolar state which involves the substituent. In the nitro-carbonyl compounds either

TABLE 1. *Ultraviolet light absorption of nitro-benzaldehydes and -acetophenones in constant-boiling ethanol.*

	Band 1		Band 2		Band 3	
Compound	$\lambda_{max.}$ (mμ)	ε	$\lambda_{max.}$ (mμ)	ε	$\lambda_{max.}$ (mμ)	ε
Unsubst. Ph·CHO	—	—	244	12,300	280	1600
o-NO_2	220	8500	252	4700	270	3600
m-NO_2	210	6800	265	11,700	—	—
p-NO_2	211	5800	265	11,400	—	—
Unsubst. Ph·COMe ...	—	—	244	11,800	278	1000
o-NO_2	205	11,000	256	4800	—	—
m-NO_2	227	22,000	~261 (infl.)	~6600	—	—
p-NO_2	218	3500	263	13,800	—	—

group may serve as the site of the negative charge in the excited state and, therefore, we consider that a competitive interaction between the two substituents occurs. This results in a marked broadening of the band in the disubstituted compounds, a slight bathochromic shift, and a reduction in the intensity of absorption to values which are, in most cases, intermediate between that of the unsubstituted compound and that of nitrobenzene.

For the *o*-nitro-compounds the intensity of band 2 is less than half the average value for the other isomers. On the other hand, there is but little change in the wavelength of the maximum. These are the characteristic features of a type 1 steric effect described by Braude and Sondheimer,[1] and we may regard either of the attached *ortho*-groups as impeding the approach of the second to that planarity with the ring which is required in the polar excited state.

Turning to band 1 we cannot explain the generally small differential substituent effects. A similar band was observed by Ungnade [7] for the halogenated nitrobenzenes where it showed no steric effects whilst the 250 mμ bands (which also appeared) did. This author regarded the 210 mμ band as derived from the 183 mμ transition of benzene in which the excited state is a dipolar form not involving the substituents as possible charge sites (*i.e.*, the ring alone is polarised). This is also the view taken by Bowden and Braude [6] for other examples of a similar band. Steric effects are also absent from the present bands and we accept Ungnade's explanation.

The outstanding feature of the results for band 1 is the slight bathochromic shift and large increase of intensity shown by *m*-nitroacetophenone. Whilst Ungnade did not record the maxima of his 210 mμ bands, the steepness of his absorption curves at *ca.* 220 mμ suggests that a similar "*meta*-effect" may be present in the halogenonitrobenzenes.

Mononitrochalcones.—On the basis of previous work [2,8] it may be assumed that the chalcones prepared in the present study are *trans*-isomers. The apparent failure of the second band to appear in most of the nitro-compounds (see Table 2) is characteristic of *trans*-isomers, and is probably due to its being overwhelmed by band 1 or 3 as these show increased intensities relative to the parent molecule. In a similar way the intensity of band 2 in *p'*-nitrochalcones has swamped its first band.

[5] Braude, *Ann. Reports*, 1945, **42**, 125.
[6] Bowden and Braude, *J.*, 1952, 1068.
[7] Ungnade, *J. Amer. Chem. Soc.*, 1954, **76**, 1601.
[8] Kuhn, Lutz, and Bauer, *ibid.*, 1950, **72**, 5058; Lutz and Jordan, *ibid.*, p. 4090; Black and Lutz, *ibid.*, 1953, **75**, 5990.

The wavelength of band 1 is reasonably constant throughout the three series of compounds (chalcones, aldehydes, and ketones), except for *m*-nitroacetophenone and *m'*-nitrochalcone. Moreover, the intensities observed in the chalcones are free from steric effects and are approximately double the values observed for the single-ring compounds. This consistency leads to the conclusion that the band has the same origin in the three series, *viz.*, it is an *E*-type transition of the benzene nuclei.

TABLE 2. *Ultraviolet light absorption of mononitrochalcones in constant-boiling ethanol.*

Subst. in	Band 1		Band 2		Band 3	
Ph·CH:CH·COPh'	$\lambda_{max.}$ (mμ)	ε	$\lambda_{max.}$ (mμ)	ε	$\lambda_{max.}$ (mμ)	ε
Unsubst.	209	9800	227	9400	309	21,000
o-NO_2	210	15,000	—	—	276	19,500
m-NO_2	215	13,000	—	—	290	27,000
p-NO_2	210	15,000	—	—	315	30,000
o'-NO_2	218	15,000	—	—	298	23,000
m'-NO_2	237	20,500	—	—	317	21,500
p'-NO_2	—	—	268	17,000	321	20,000

The band found with *m'*-nitrochalcones is quite similar to that shown by the *meta*-substituted ketone and we consider that it arises from the same transition in both cases, *i.e.*, in the chalcone it is partial chromophore band. Its position is reminiscent of the bands shown by αβ-unsaturated ketones (*ca.* 230 mμ) discussed by Schubert and Sweeny,[9] and by Mecke and Noack,[10] though its intensity is higher than normal (*ca.* 12,000) for such compounds. Whilst the intensity difference could be reasonably explained, we hesitate to advance firmly this explanation of the anomalous absorption.

We accept the failure of band 2 to appear in most of the compounds of this series as evidence of a suppression relative to the parent compound, though not necessarily as strongly as the tabulated results suggest owing to the increased breadth of band 3. The results are then comparable with those for the nitro-aldehydes and -ketones where the *K*-band was also depressed and showed the expected steric effects. The anomalous behaviour of *p'*-nitrochalcone is matched by the similar behaviour of *p*-nitroacetophenone, since in both these compounds band 2 is stronger than in other isomers and is even stronger than in its unsubstituted parent compounds. Therefore, in these two cases the *p*-nitro-group assists the transition which cannot be normal carbonyl-ring polarisation such as is involved in the benzoyl chromophore.

The features of band 3 are more constant throughout the *o'*- *m'*- *p'*-series (benzoyl substituted) than through the *o*- *m*- *p*-series (cinnamoyl substituted), giving support to Black and Lutz's conclusion [2] that this is a partial chromophore band of the cinnamoyl group. The *ortho*-compound shows normal steric-hindrance effects which are confirmed by examination of models.

It has been pointed out by Ferguson and Barnes [11] that negative groups in the cinnamoyl ring should tend to depress the polarisation of the cinnamoyl system, leading to changes in band 3 similar to that described for the *o*-nitro-group. It is, therefore surprising to find that *m*-nitro-group has a greater depressing effect (implying greater electron-attraction) than the more favourably placed *p*-nitro-group which even slightly enhances the ease and probability of this transition. This anomaly finds a parallel in the kinetic study of these compounds (see following paper) and is discussed there. The *p*-nitro-group may here be introducing a contribution from the *p*-nitrostyryl chromophore as suggested by Black and Lutz [8] for *cis-p*-nitrochalcone.

Dinitrochalcones.—In the absence of definite evidence concerning the configuration of the dinitro-compounds, which were prepared by the method used for the *trans*-mononitro-series, we assume that they also were the *trans*-forms. The striking effect of disubstitution

[9] Schubert and Sweeny, *J. Amer. Chem. Soc.*, 1955, **77**, 2297.
[10] Mecke and Noack, *Angew. Chem.*, 1956, **68**, 150.
[11] Ferguson and Barnes, *J. Amer. Chem. Soc.*, 1948, **70**, 3907.

is the emergence of band 2 as the strongest band in the spectrum (see Table 3). This is so pronounced that band 3 is frequently swamped, although band 1 is not reported in Table 3 it appears at an almost constant wavelength of 210 mμ with intensities between 15,000 and 20,000.

It is immediately apparent that the nature of band 2 is controlled by the substituent in the benzoyl group. Thus the three compounds containing the *m'*-nitro-group show

TABLE 3. *Ultraviolet light absorption of dinitrochalcones in constant-boiling ethanol.*

Subst. in Ph·CH:CH·COPh′		Band 2 $\lambda_{max.}$ (mμ)	Band 2 ε	Band 3 $\lambda_{max.}$ (mμ)	Band 3 ε	Subst. in Ph·CH:CH·COPh′		Band 2 $\lambda_{max.}$ (mμ)	Band 2 ε	Band 3 $\lambda_{max.}$ (mμ)	Band 3 ε
o	*o'*	255	21,900	—	—	*p*	*m'*	245	16,500	315	22,000
m	*o'*	267	24,500	—	—	*o*	*p'*	265	19,500	—	—
p	*o'*	—	—	307	22,500	*m*	*p'*	272	21,000	305 †	14,000
o	*m'*	245	23,500	300 *	10,000	*p*	*p'*	270	22,500	—	—
m	*m'*	247	16,500	317	28,500						

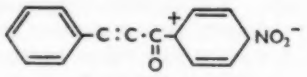
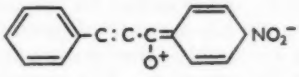
* Weak inflexion. † Strong inflexion.

similar bands; there is no noticeable effect from the other nitro-group as this changes its position in the cinnamoyl ring. Moreover, there is a similarity between these bands and the anomalous band 1 appearing in both *m*-nitroacetophenone and *m'*-nitrochalcone.

An identical comparison may be made with the spectra of the *p'*-dinitro-compounds and band 2 of *p'*-nitrochalcone. We conclude from this consistency that the same transition is involved in both the mono- and the di-nitro-series. It should be noted that we have traced anomalies, first noticed in *m*- and *p*-nitroacetophenone, through all compounds containing these nitro-carbonyl systems. The band increases in intensity and decreases in wavelength from the ketone, through the chalcone, to the dinitrochalcone; *i.e.*, as the other group attached to carbonyl-carbon becomes more electronegative. We cannot, therefore, consider that the transition involved is a normal polarisation of the benzoyl group, which would otherwise fit the results. It seems more likely that a normal polarisation of the nitro-group might be involved.

Band 3 is regarded as arising from the cinnamoyl group transition which gives rise to band 3, of the same wavelength, in the mononitro-compounds. Thus the three instances where it appears (*po'*, *mm'*, and *pm'*) contain the *m*- or *p*-nitrocinnamoyl group, being those which showed enhanced values for band 3 in the mononitrochalcones. The intensities of the present bands are lower than the corresponding bands of the *m*- and *p*-nitrochalcones; this is attributed to the general depression of polarisability of carbonyl groups by the second nitro-group.

It is noteworthy that the appearance of band 3 is accompanied by a decrease in the intensity of band 2. Thus structures which favour the transition involved in band 3 are

(I)   (II)

more resistant to the transition involved in band 2. This supports our conclusion that band 2 may involve transition to an excited state of the structure (I) or (II).

EXPERIMENTAL

The chalcones were prepared by the standard method of shaking equimolar quantities of the appropriate aldehyde and ketone in methanol *ca.* 0·2 molar in sodium hydroxide. After ice-cooling and filtration the solid product was washed with methanol before repeated recrystallisation.

Chalcone	Solvent	M. p.	Chalcone	Solvent	M. p.	Chalcone	Solvent	M. p.
Unsubtd....	EtOH	57·5°	*p*'-NO_2	EtOH	147—148°	*mm*'-$(NO_2)_2$	Ac_2O	206—208°
o-NO_2	,,	119*	*oo*'-$(NO_2)_2$...	,,	133—134	*pm*'-$(NO_2)_2$	,,	205
m-NO_2	,,	141	*mo*'-$(NO_2)_2$	,,	124—125	*op*'-$(NO_2)_2$...	Benzene	121—122
p-NO_2	,,	162—163	*po*'-$(NO_2)_2$	,,	178—179	*mp*'-$(NO_2)_2$	AcOH	197—199
o'-NO_2	,,	125—126	*om*'-$(NO_2)_2$	AcOH	160—161	*pp*'-$(NO_2)_2$...	,,	129 †
m'-NO_2 ...	,,	130·5						

* Air-drying at 100° increased the m. p. to *ca.* 125° with accompanying darkening.
† Commencement of melting indefinite.

The aldehydes and ketones were purchased, except *o*-nitroacetophenone which was prepared by the method in *Organic Syntheses*.[12]

Absorption Spectra.—The spectra were determined upon freshly prepared solutions in constant-boiling ethanol, at dilutions giving optical densities of *ca.* 0·6 at the maxima. The solubilities of the substituted chalcones in constant-boiling alcohol are very small at room temperature and prolonged shaking was necessary to obtain standard solutions. In certain difficult cases solutions *ca.* 0·0003M were prepared directly in 250 ml. of solvent. The *mm*'- and *pp*'-dinitrochalcones resisted even this treatment and the samples had first to be dissolved in dioxan, the initial solution being diluted with constant-boiling ethanol so that the spectrum was actually measured in 1% dioxan–alcohol with a similar control. The controls examined against alcohol showed no absorption.

Measurements were made with both a Unicam SP500 and a Hilger Uvispek spectrophotometer with concordant results.

WEST HAM COLLEGE OF TECHNOLOGY, LONDON, E.15. [*Received, November 30th*, 1956.]

[12] *Org. Synth.*, 1950, **30**, 70.

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392. *The Base-catalysed Decomposition of Mononitrochalcones in Aqueous Alcohol.*

By E. A. WALKER and J. R. YOUNG.

The velocity constants and activation energies for the hydrolytic decomposition of chalcone and its six ring-substituted mononitro-derivatives in constant-boiling ethanol have been measured. The rate is proportional to the concentration of added base; no acid-catalysis is observed.

All substituents (with the exception of *p*-NO_2) reduce the activation energy and this, with the kinetics, suggests that the rate-determining step is attack by hydroxyl ion. A probable mechanism is suggested.

The anomalous behaviour of the *p*-nitro-group, which has a parallel in the spectra of these compounds, is discussed.

CHALCONES (benzylideneacetophenones) offered a suitable system with which to extend the work of Lucas *et al.*[1] on the addition of water to a double bond conjugated with a carbonyl group. In addition, the effect of substituents may be compared under conditions of direct and crossed conjugation between the nucleus and the reaction centre.

Chalcone and the six mononitrochalcones were decomposed in *ca.* 5×10^{-4}M-solution in constant-boiling ethyl alcohol containing sodium hydroxide as catalyst. The reactions were followed by removing samples and measuring the optical density (K) at the long-wavelength maximum of the chalcone after suitable dilution. The observed values of K were corrected for product absorption where necessary, and plots of log $K_{corr.}$ against time established the reaction order and enabled velocity constants to be calculated.

In all cases the log K plots were linear up to at least 20% of total reaction. Beyond this a curvature appeared which was consistent with an approach to equilibrium. Attempts to follow the equilibrium gave unsatisfactory results which were attributed to

[1] Lucas, Stewart, and Pressman, *J. Amer. Chem. Soc.*, 1944, **66**, 1818.

various side-reactions involving the initial products. On the other hand, spectrographic analysis of the final reaction mixtures using additional wavelengths gave satisfactory agreement with the expected concentrations of free aldehyde and ketone.

The velocity constant k' calculated from the slope of the linear plots was shown to be proportional to the concentration of sodium hydroxide present (0·05—0·2M). Thus the reaction was of second order and the law, Rate $= k'$[Chalcone] $= k$[Chalcone][NaOH], was obeyed. Within the temperature range 25—55° the plots of log k against 1/Temperature (°K) were linear to the expected accuracy and gave the activation energies. The full results are in the Table.

Kinetic data for the decomposition of chalcones in constant-boiling ethanol catalysed by sodium hydroxide.

Compound Subst. Ph·CH:CH·COPh′	Velocity constants 10^2k (mole^{-1} l. min.$^{-1}$) 25°	35°	45°	55°	E_a(kcal.)	log PZ
Nil	—	0·45	1·2	3·4	20·0	10·9
o-NO_2	5·9	12·0	23·0	—	12·6	6·3
m-NO_2	1·6	4·6	12·0	—	19·1	10·5
p-NO_2	1·1	3·5	9·9	—	20·3	11·3
o′-NO_2	0·62	1·8	4·3	—	18·1	9·4
m′-NO_2	1·9	6·0	17·0	—	20·0	11·2
p′-NO_2	2·9	8·1	21·0	—	18·4	10·2

The effect of catalysis by 0·1M-hydrochloric acid was investigated for each compound, without detectable results. Unsuccessful attempts were made in some cases to follow the condensation from the aldehyde and ketone to the chalcone, the presence of the nitro-group in either of the simple compounds leading to an early equilibrium. More success attended measurements upon the system benzaldehyde–acetophenone where a velocity constant of approximately 14 mole^{-1} l. hr.$^{-1}$ was found at 55° (Coombes and Evans's data [2] give 15·0 for this constant), but even here an equilibrium was being approached.

The net reaction studied is:

$$\text{Ph·CH:CH·COPh′} + H_2O \longrightarrow \text{Ph·CHO} + \text{Ph′·COMe}$$

Since water was in excess in the solvent used, its concentration did not enter the rate equation. The observed proportionality to the sodium hydroxide concentration is consistent with the attack of the reactant anion on the β-carbon atom of the double-bond conjugated to the carbonyl group, *e.g.*:

$$(1)\ (H_2O + EtO^- \rightleftharpoons EtOH + OH^-)$$

$$(2)\ \text{Ph·CH:CH·COPh′} + OH^- \rightleftharpoons \text{Ph·CH(OH)·}\bar{\text{C}}\text{H·COPh′}\quad (A)$$

This conclusion is analogous to the proposal made by Ingold [3] on general grounds for the rate-determining stage of typical Michael reactions and supported by the results of Kamlet and Glover [4] in such an instance.

The interest of the reaction concerns the fate of the ion (*A*). Thus we may consider that it accepts a proton from a solvent molecule to form the ketol, which then breaks down by the accepted mechanism.[5] This possibility leads to the scheme:

$$(3)\ \text{Ph·CH(OH)·}\bar{\text{C}}\text{H·COPh′} + ROH \rightleftharpoons \text{Ph·CH(OH)·CH}_2\text{·COPh′} + OR^-$$

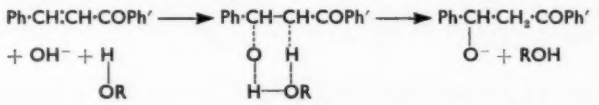
$$(4)\ \text{Ph·CH(OH)·CH}_2\text{·COPh′} + OR^- \rightleftharpoons \text{Ph·CH(O}^-\text{)·CH}_2\text{·COPh′} + ROH \qquad (B)$$

$$(5)\ (B) \rightleftharpoons \text{Ph·CHO} + {}^-\text{CH}_2\text{·COPh′}$$

$$(6)\ {}^-\text{CH}_2\text{·CO·Ph} + ROH \rightleftharpoons \text{CH}_3\text{·COPh′} + OR^-$$

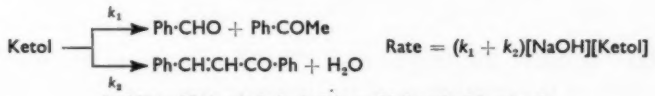
[2] Coombes and Evans, *J.*, 1942, 1295.
[3] Ingold, "Structure and Mechanism in Organic Chemistry," Bell, London, 1953, p. 693.
[4] Kamlet and Glover, *J. Amer. Chem. Soc.*, 1956, **78**, 4556.
[5] Ingold, *op. cit.*, p. 682.

Alternatively we may consider that, since the intermediate ions (*A*) and (*B*) differ only in the position of a single hydrogen atom, there is a direct route from (*A*) to (*B*) not involving the ketol. Such a route might be provided if the transition state for reaction (2) involves a solvent molecule, *e.g.* :



This suggestion s taken from Laidler and Landskroener [6] who find theoretical support for the occurrence of such forms in, for example, base-catalysed ester hydrolysis.

Against the attractiveness of the proposal must be placed Noyce and Pryor's results,[7] which, in addition to providing kinetic evidence for the occurrence of the ketol in the acid-catalysed condensation of benzaldehyde and acetophenone, include a synthesis of this compound (by an indirect route) and measurement of its acid- and base-catalysed dehydration and decomposition. Their values for the base-catalysed reactions are :



At 26° in 90% ethyl alcohol $k_1 = 11{\cdot}5$ mole^{-1} l. min.$^{-1}$.
$k_2 = 3{\cdot}1$,,

Under the same conditions the condensation of benzaldehyde and acetophenone has a rate constant of $4{\cdot}5 \times 10^{-2}$, whilst our results in constant-boiling alcohol (*ca.* 96%) give a calculated value of $1{\cdot}5 \times 10^{-3}$ for the decomposition of chalcone at this temperature. The rates of the ketol reactions are thus sufficiently large by comparison to ensure that the rate-controlling steps of the base-catalysed condensation and chalcone decomposition do not involve ketol. On the other hand, they establish a degree of stability for the ketol which suggests that it is likely to be formed at least in small quantity. It would be interesting to examine these reactions more closely than we have been able to do, with a view to establishing the route taken or the proportions of molecules following alternative routes between chalcone and products.

Effects of Substituents.—The effects of then itro-substituents are consistent with the suggestion that hydroxyl-ion attack is rate-determining. Thus in most cases the energy of activation is lower than that of the unsubstituted compound.

The mesomeric effect of the nitro-group will not be called into operation from substituents in the ring remote from the carbonyl group and we may expect reductions of activation energy to be produced by the inductive effects alone. E_A for the *meta*-compound is 1 kcal. lower than for the parent, and this value sets the magnitude of the differences to be expected. On this basis the *ortho*-group is exerting an enhanced effect and the *para*-group a reduced electron attraction. The same observation holds when the velocity constants of the *meta*- and *para*-compounds are compared; this is desirable in this case since the estimated accuracy of the E_A is $\pm 0{\cdot}6$ kcal.

We explain the *ortho*-anomaly on steric grounds. Thus in this compound mutual steric hindrance between side-chain and nitro-group force both structures out of the ring-plane. Thus the required polarisation of the carbonyl group and the adjacent double bond (form I) is not reduced by interaction with the ring π-electrons, *i.e.*, the electron density on the β-carbon atom is lower than it would be were the *p*-orbitals of this atom perpendicular to the ring plane as required in the polarised cinnamoyl form (form II).

[6] Laidler and Landskroener, *Trans. Faraday Soc.*, 1956, **52**, 200.
[7] Noyce and Pryor, *J. Amer. Chem. Soc.*, 1955, **77**, 1397.

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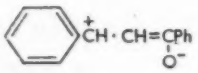
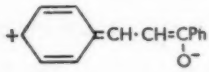
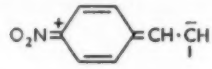
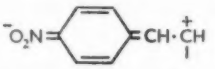
Moreover, the inductive effect of the nitro-group is here acting from the nearest position to the side-chain. Thus the apparent energy of activation has the very low value of 12·6 kcals. whilst the simultaneously low steric factor reflects the difficulty of approach to the β-carbon atom.

(I)   (II)

The behaviour of the *p*-nitro-group in showing either no effect or possibly a very small $+I$ effect was also evident in the spectrum of this compound, where it exerted a slight bathochromic influence upon the 300 mμ band (see ref. 8). Such anomalies in the effect of the nitro-group are not unknown and have been recently discussed by Braude and Waight.[9] These workers suggest that in the *p*-nitrostyryl system the styryl polarisation may make a greater contribution to the ground state than the nitro-polarised form, *i.e.*, (III) contributes more than (IV), leading to smaller effects from the *p*-nitro-group than

(III)   (IV)

were expected. However, we consider that in the present system the contribution from form (IV) depresses the polarisation of the carbonyl group to give (I), leading to the slightly higher activation energy of the *para*- than of the *meta*-compound. The spectrographic anomaly (see ref. 8) is explicable if the 300 mμ band for the *para*-compound arises from superimposed cinnamoyl and *p*-nitrostyryl absorption; this complexity is rendered more likely if form (IV) makes a relatively large contribution to the ground state, as assumed above.

In the *o'*-, *m'*-, and *p'*-compounds the substituent effects are more regular. The absence of measurable effect from the *m'*-group and the approximately equal diminutions of E_A caused by the *o'*- and *p'*-substituents are strong evidence in favour of electromeric assistance in the reaction. On the other hand, it is impossible to write conventionally bonded excited states for *o'*- and *p'*-nitrochalcones, which show nitro-group polarisation and a formal positive charge on the β-carbon atom. In spite of the difficulty, we believe that a rather weak electromeric effect is being transmitted to the β-carbon atom *via* the cross-conjugated carbonyl group in these compounds, the inductive effects being negligible.

Experimental

Preparation.—The chalcones were prepared by the standard method outlined earlier.[8] Constant-boiling ethyl alcohol, used as solvent for kinetic work, was prepared in large quantity by Baker and Hemming's method.[10]

Catalyst Solution.—The catalyst solution was 0·5M-sodium hydroxide in the solvent alcohol. It was prepared in small quantities and not stored for any length of time. A slight excess of the hydroxide pellets was dissolved in 100 ml. of constant-boiling alcohol; this solution showed a carbonate deposit which was removed by drawing the solution off through a sintered-glass filter into a protected flask. The strength of the final solution, determined by titration with standard hydrochloric acid, showed no carbonate by differential titration.

Rate Measurement.—The chalcone (2—4 mg.) in a 25 ml. flask was treated with *ca.* 19 ml. of solvent and immersed in a thermostat at the reaction temperature; catalyst and pure solvent were similarly stored. Dissolution of the chalcone was normally complete in 30 min. by which time the contents had reached the bath-temperature. Catalyst solution (5 ml.) was added

[8] Walker and Young, preceding paper.
[9] Braude and Waight, *J.*, 1953, 419.
[10] Baker and Hemming, *J.*, 1942, 191.

and the volume rapidly made up to the mark with solvent at the bath-temperature. The whole was mixed by short vigorous shaking. About 5 min. were allowed for the reaction to settle down after mixing, and the first 1 ml. sample was then removed for analysis, followed by others later. All samples were run into *ca.* 8 ml. of solvent in a 10 ml. graduated flask, the time intervals being measured from the commencement of delivery. The diluted solution was made up to 10 ml. and the optical density of this solution was measured (Unicam SP500 Spectrophotometer) in a 0·5 cm. silica cell at the $\lambda_{max.}$ for the chalcone against a control of pure solvent and at a constant slit width of 0·1 mm.

Variations in the catalyst concentration were made both by changing the concentration of the catalyst solution and by altering the amount added to the reaction mixture.

The results for a typical experiment are given below.

o'-Nitrochalcone at 35°.

0·0032 g. in 25 ml. of solution containing 5 ml. of 0·357M-NaOH. 1 ml. samples, determined at 298 mμ, gave the following readings.

Time (min.)	0	7	14	21	28	35	42	50	57	64
$\log I_0/I\ (=K)$	0·563	0·553	0·544	0·533	0·521	0·511	0·503	0·490	0·484	0·474
$-\log K$	0·249	0·257	0·264	0·273	0·283	0·291	0·298	0·309	0·315	0·324

$k' = k$[Catalyst] $= 1{\cdot}15 \times 10^{-3}$.
$k = 1{\cdot}61 \times 10^{-2}$ mole^{-1} l. min.$^{-1}$ (uncorr.).

Correction for k. ε at 298 mμ are: *o'*-nitrochalcone 22,600; Ph·CHO 150; *o*-$NO_2{\cdot}C_6H_4{\cdot}COMe$ 1300. Thus:

$$K_{corr.} = K_0 - \Delta K_{obs.}[22{,}600/(22{,}600 - 150 - 1300)]$$
$$= K_0 - 1{\cdot}07\Delta K_{obs.}$$

Whence, from the Table: $k_{corr.} = 1{\cdot}76 \times 10^{-2}$ mole^{-1} l. min.$^{-1}$.

The individual measurements of k showed standard deviations of ±3% (*e.g.*, for chalcone $10^2 k_{35}$ were 0·436, 0·449, 0·459, and 0·454). This rather low accuracy arises from two causes: first, the correction procedure adopted is not strictly accurate since it assumes that the K_0 (*i.e.*, the optical density at zero time) is entirely due to chalcone whereas some slight reaction has already occurred; this reduces the final k. Secondly, there is curvature towards infinite slope of the plot of log K against time which is caused by the approach to equilibrium; in most cases the early linear portion was unmistakable but in others a tendency to curvature could be detected after 15% change; in order to avoid this the measurements had to be restricted to the first 20% of reaction which meant compressing the whole experiment into an optical-density range of approx. 0·1 (*i.e.*, from 0·5 to 0·4) with a consequent loss of accuracy.

The few experiments on acid-catalysis employed a similar method and a catalyst solution of 0·5M-hydrogen chloride in the kinetic solvent, which was prepared by passing dry gas into the constant-boiling alcohol. For example, sealed samples consisting of an acid chalcone solution (7×10^{-4}M-chalcone, 0·1M-HCl) and a neutral solution of the same concentration were kept at 35° for 30 days. Spectrographic analysis of both series at four selected wavelengths showed no significant absolute or relative changes throughout this period. A complete spectrum at the end indicated a possibly slightly greater degree of decomposition in the neutral sample. The experiments on the nitrochalcones were shorter and simpler, but just as conclusive.

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393. *Isotope Effects in Diffusion Cross-sections for Flexible Hydrocarbons.*

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Mass diffusion coefficients have been measured for straight- and branched-chain C_7- and C_8-alkanes. Comparisons between hydrogen, deuterium, and helium as carrier gases have permitted estimates of the relative importance of low mass and of high internal energy quanta in leading to anomalously large collision "diameters" (the "hydrogen effect") for flexible hydrocarbons. Nitrogen and argon have also been used as carrier gases for reference. Results show anomalies which are in the sequence $H_2 > D_2 > He$.

Previous researches in momentum and mass transport in gaseous hydrocarbons [1,2] have indicated that in the gas phase flexible hydrocarbon molecules adopt an average configuration which is substantially crumpled. Relative efficiencies for transference of vibrational energy in ultrasonic waves to ethylene by collision with different hydrocarbons roughly parallel the molecular flexibilities.[3] Another method of studying inelastic collisions involving transfers of translational to internal energy is to measure relative collision "diameters" in mass transport. Different carrier gases used with the same flexible hydrocarbons lead to different apparent collision diameters. These can be attributed to variations in molecular "roughness." An enlargement of flexible hydrocarbons observed in diffusion with hydrogen has been termed the "hydrogen effect." [2,4] It is still uncertain how far such effects are due to the low mass of the hydrogen, or to its large quanta of rotational internal energy. Researches described below give, for the hydrocarbons studied previously, comparative results with hydrogen and with deuterium, which exert effectively similar force fields but differ in mass and rotational quanta. Comparisons are also made between deuterium and helium, where the mass is the same but the internal energies and force fields differ. Nitrogen has been used as reference carrier gas. Argon was also used in a few experiments though the relatively large atomic mass of argon makes it less satisfactory experimentally.

Experimental

Materials.—n-*Octane.* This was part of the pure sample used previously [2] and had $n_D^{20\cdot3}$ 1·3975.

2 : 2 : 4-*Trimethylpentane,* n-*heptane, and* 2 : 4-*dimethylpentane.* These were gifts from the British Petroleum Co. to whom thanks are offered for their continual help in supplying compounds of high purity. Samples of the first two were stored over sodium wire, refluxed, and finally distilled. The dimethylpentane was used as received.

Refractive indices were, respectively, $n_D^{19\cdot8°}$ 1·3918, $n_D^{20\cdot0°}$ 1·3879, and $n_D^{20\cdot4°}$ 1·3816.

Helium. This was provided by the British Oxygen Company. Limits of impurities were stated to be carbon dioxide ~2 v.p.m.; oxygen less than 10 v.p.m.; other carbonaceous compounds as CO_2 ~2 v.p.m. To remove carbon dioxide and other condensable impurities, the gas was passed through a liquid-air trap packed with glass wool [5] attached to the apparatus (Fig. 1).

Deuterium. This was from two sources, (*a*) a kind gift from Dr. K. E. Weale of this Department which had been prepared by electrolysis of deuterium oxide,[6] and (*b*) as a check, a sample of deuterium was prepared *in situ* by treating 99·75% deuterium oxide with powdered magnesium

[1] McCoubrey, McCrea, and Ubbelohde, *J.*, 1951, 1961.
[2] Cummings and Ubbelohde, *J.*, 1953, 3751.
[3] McGrath and Ubbelohde, *Proc. Roy. Soc.*, 1954, *A*, **227**, 1.
[4] Cummings, McLaughlin, and Ubbelohde, *J.*, 1955, 1141.
[5] Ubbelohde, *J.*, 1933, 972.
[6] Lachowicz, Newitt, and Weale, *Trans. Faraday Soc.*, 1955, **51**, 1198.

at 490°. The method was based on that described by Knowlton and Rossini [7] for a reduced scale (Fig. 1).

In Fig. 1, *C* is a Pyrex capsule containing deuterium oxide which had been degassed by repeated freezing and melting under a vacuum. The Pyrex reaction tube *E* containing magnesium powder of graded fineness was heated electrically. A tight packing of purified glass wool at the top of the magnesium packing and in the liquid-air trap L_3 prevented the passage of oxide particles into the main section of the apparatus. The magnesium column was baked under a vacuum at 480—500° for a day before the reaction was carried out. The capsule *C* was then fractured by placing liquid oxygen around the outer wall, and the deuterium evolved initially was taken off in the pumps before the diffusion apparatus was filled.

Results with stored deuterium agreed within ½% with those for the specially prepared deuterium in the case of 2 : 2 : 4-trimethylpentane–deuterium. Stored deuterium was therefore used for the remaining measurements.

FIG. 1.

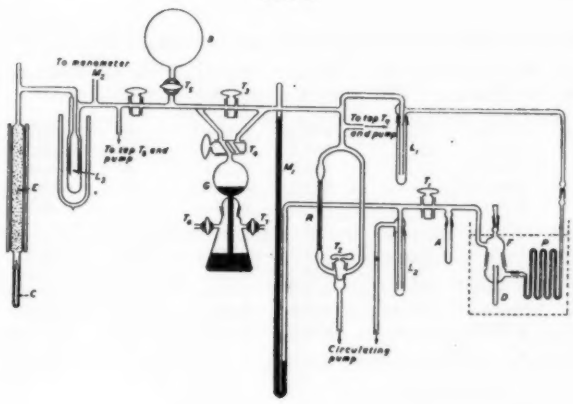
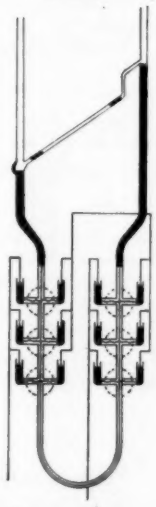


FIG. 2.



Hydrogen, nitrogen, and argon were used as supplied by the British Oxygen Company.

Apparatus and Technique.—The Stefan method of measuring gaseous interdiffusion was employed. (A recent review of diffusion techniques is given by Wilke and Lee.[8])

(*a*) For measurements with hydrocarbons and permanent gases the technique described previously [2] was used. The thermostat temperature was measured by means of a N.P.L. certified mercury-in-glass thermometer reading to 0·02° C.

The diffusion tubes used were of internal bore 2·5—3 mm. The measured diffusion coefficient was found by the conventional technique to be independent of flow rate of the carrier gas down to 50 c.c./min. The lowest flow rate previously investigated [2] was 100 c.c./min. Low flow rates are particularly convenient when circulation of rare gases is necessary, as below.

(*b*) For measurements with deuterium and helium it was necessary to recycle the gas through a closed system capable of being evacuated to $<10^{-4}$ mm. Hg. Initially a wholly enclosed centrifugal blower was employed, using a magnetic induction drive. This was not adequate owing to trouble with bearings. A more satisfactory form of apparatus employed an electromagnetically operated Sprengel-type pump having no mechanically moving parts.[9] This consisted of six electromagnetic units (Fig. 2). Current was supplied through the platinum seals from a bridge rectifier and step-down transformer (11·5 v) fed from the a.c. mains through a Variac transformer. With permanent magnets of field strengths 5000—6000 gauss,

[7] Knowlton and Rossini, *J. Res. Nat. Bur. Stand.*, 1937, **19**, 605.
[8] Wilke and Lee, *Ind. Eng. Chem.*, 1955, **47**, 1253.
[9] Cf. Puddington, *Canad. J. Technol.*, 1951, **29**, 311.

a d.c. current of about 17 amp. through each unit gave a total pumping speed of about 100 c.c./min. No serious loss of performance was found with a moderate flow resistance in the apparatus; this permitted the inclusion of a specially calibrated rotameter R (Fig. 1) to provide a check on flow rates.

The hydrocarbon to be studied was degassed under a vacuum in A and was distilled into the diffusion tube D. After preliminary "washing" of the walls with the gas to be used and pumping out, the apparatus was filled with gas to about one atmosphere, the Töpler pump G being used if necessary, and the hydrocarbon was cautiously melted. Taps T_3 and T_4 were closed, liquid oxygen was placed around the traps L_1 and L_2, and circulation of the gas at 90—100 c.c./min. commenced. The copper preheater P (path 250 cm.) and the diffusion cell F were then placed in a thermostat ($\pm 0{\cdot}02°$); measurements of the rate of fall in the liquid level as in (*a*), and readings of pressure on M_1 and of thermostat temperature were made every half-hour. At least two hours were allowed for attainment of a steady-state condition before readings were recorded. From measurements of the rate of drop in level of hydrocarbon, calculations of the diffusion coefficient D_{12} were made for hydrocarbon 2 in carrier gas 1, by conventional procedures.

Results are in Table 1.

TABLE 1. *Diffusion coefficients of paraffins in various carrier gases.*

Carrier gas	Temp. (° K)	D_{12} (cm.² sec.⁻¹)	No. of obsns.	Precision of D ($\pm$)	Carrier gas	Temp. (° K)	D_{12} (cm.² sec.⁻¹)	No. of obsns.	Precision of D ($\pm$)
		n-Octane					*n*-Heptane		
N_2	303·1	0·0726	9	0·0012	N_2	303·3	0·0740	19	0·001
H_2	303·2	0·277	6	0·003	H_2	303·1	0·283	6	0·0023
D_2	303·2	0·208	8	0·0005	D_2	303·2	0·218	18	0·0005
He	303·2	0·248	18	0·0023	He	303·2	0·265	16	0·0008
A	303·2	0·0587	7	0·0018	A	303·2	0·0658	12	0·0010
	2 : 2 : 4-Trimethylpentane					2 : 4-Dimethylpentane			
N_2	303·1	0·0713	8	0·0014	N_2	303·1	0·0744	23	0·0007
H_2	303·1	0·292	20	0·0025	H_2	303·3	0·297	14	0·0034
D_2	303·2	0·212	26	0·0004	D_2	303·2	0·224	16	0·0003
He	303·2	0·253	27	0·0007	He	303·2	0·263	16	0·0006
A	303·2	0·0599	10	0·0003	A	303·2	0·0655	8	0·0003

Discussion

Fairly satisfactory treatments are available for the description of transport phenomena in monatomic and simple polyatomic gases.[10,11] Larger molecules, in general, possess features which make less justifiable, in varying degrees, the assumptions used with atoms and simpler molecules. Consequently, it becomes more difficult to relate force constants, deduced by kinetic theory from transport properties, with detailed molecular geometry. Calculation of the parameters is usually quite straightforward but the problem lies in interpreting them in terms of molecular behaviour. Two main methods of approach may be used in which inadequacies in the application of simple theory do not vitiate the conclusions reached:

(1) Where a series of molecules of closely similar structure depart to much the same extent from the simplest idealised models of kinetic theory, observed trends in formal kinetic-theory parameters derived from experimental results give significant relative molecular sizes, or relative collision areas, in such series.

(2) Instead of the simplest idealised models, models including approximations of higher order may be applied in calculating experimental parameters. Relative deviations from predicted behaviour may again be examined through the series of closely related molecules. Effects of differences of structure on the significance of the higher approximations can become apparent in this way.

[10] Chapman and Cowling, "The Mathematical Theory of Non-Uniform Gases," Cambridge Univ. Press, 2nd Ed., 1954.

[11] Hirschfelder, Curtiss, and Bird, "The Molecular Theory of Gases and Liquids," Wiley, New York, 1954.

Each of these methods has been used in previous analyses of experimental results for hydrocarbons.[4, 12] In the present work a similar method of approach is used; collision "parameters" are defined on the basis of the formulæ of kinetic theory for idealised models, and values deduced are examined for hydrocarbons of similar structure.

The measured diffusion coefficients in Table 1 have been analysed on the basis of two molecular models, *viz.*, the rigid-sphere model and a model assuming the Lennard-Jones 6 : 12 potential. The rigid-sphere diameter σ_{12} is defined by the standard formula :[10]

$$\left[D_{12}\right]_1 = \frac{3}{8n\sigma_{12}^2}\left\{\frac{kT(m_1+m_2)}{2\pi m_1 m_2}\right\}^{\frac{1}{2}} \quad . \quad . \quad . \quad . \quad . \quad (1)$$

where σ_{12} is the heteromolecular collision diameter, while the corresponding diameter for the Lennard-Jones potential is given by :

$$\left[D_{12}\right]_1 = \frac{3}{8n\sigma_{12}^2}\left\{\frac{kT(m_1+m_2)}{2\pi m_1 m_2}\right\}^{\frac{1}{2}} \cdot \frac{1}{W^1(1\,;\ kT/\varepsilon_{12})} \quad . \quad . \quad . \quad . \quad (2)$$

where $W^1(1\,;\ kT/\varepsilon_{12})$ is the collision integral for mass transport. Such integrals are tabulated by Hirschfelder and his co-workers.[11, 13]

Values of the collision diameter for the hydrocarbon are derived from σ_{12} by using values of σ_{11} for the carrier gas from viscosity data listed below (Table 2). Use is made of the empirical relations,

$$\sigma_{12} = \tfrac{1}{2}(\sigma_{11} + \sigma_{22}) \quad . \quad . \quad . \quad (3); \qquad \varepsilon_{12} = (\varepsilon_{11}\varepsilon_{22})^{\frac{1}{2}} \quad . \quad . \quad . \quad (4)$$

In the case of the Lennard-Jones potential, values of ε_{22}/k for the hydrocarbons from viscosity data were used in the evaluation of σ_{22}. For the C_8-hydrocarbons values of viscosities previously measured in this programme were used.[14] For the C_7-hydrocarbons viscosity results of Lambert and co-workers [15] were fitted to a 6 : 12 potential. With the 6 : 12 potential the same diameter σ_{11} was used for deuterium as for hydrogen as measurements were not available for the viscosity above room temperature.

TABLE 2. *Gas-kinetic collision diameters of carrier gases.*

Gas	Rigid sphere model σ_{11} (Å)	6 : 12 Model σ_{11} (Å)	ε/k (°K)	Ref. for viscosity data
H_2	2·71	2·97	33·3	*a*
N_2	3·75	3·68	91·5	*a*
D_2	2·73	—	—	*b*
He	2·16	2·58	10·22	*c*
A	3·66	3·42	124	*c*

(*a*) Johnston and McCloskey, *J. Phys. Chem.*, 1940, **44**, 1038. (*b*) van Itterbeek and van Paemal, *Physica*, 1940, **7**, 265, 273. (*c*) Johnston and Grilly, *J. Phys. Chem.*, 1942, **46**, 938.

Consideration of the nature of the colliding molecules makes it clear that neither of these two physical models can be wholly adequate. Even if the simpler molecules of the carrier gases may be treated as rigid spheres, or as sources of centrosymmetric 6 : 12 forces, this is certainly not permissible for polyatomic hydrocarbons, especially for structures ("flexible molecules") where changes of potential energy required to effect changes of rotational configuration are small. Formally, however, the basis of definition of the parameters to be compared is quite specific.

The Hydrogen Effect with Flexible Molecules.—In accord with previous studies,[2, 4] the

[11] Cummings, McCoubrey, and Ubbelohde, *J.*, 1952, 2725.
[13] Hirschfelder, Bird, and Spotz, *J. Chem. Phys.*, 1948, **16**, 968.
[14] Cummings and McCoubrey, *J.*, 1955, 2523.
[15] Lambert, Cotton, Pailthorpe, Robinson, Scrivens, Vale, and Young, *Proc. Roy. Soc.*, 1955, *A*, **231**, 280.

kinetic-theory cross-sections for collisions of hydrocarbons with hydrogen are seen to be greater than those for the corresponding collisions with nitrogen when the hydrocarbon is flexible. In column 7 of Table 3 the quantity Δ, defined as $\sigma_{22}(H_2) - \sigma_{22}(N_2)$, has a finite positive value for the flexible hydrocarbons but has a much lower value for the stiffer molecules of equal mass. Parameters based on the Lennard-Jones potential show the same general trends.

Inadequacy of the first approximation to the coefficient of diffusion [(1) and (2) above] cannot account for a deviation in the predicted collision diameters, of more than about 0·1% for the molecules studied at concentration ratios used in the measurements. Other assumptions and approximations made in developing a practicable theory of transport properties in gases have been examined as possible sources of the differences observed.[4] Further reasons for rejecting quantum effects as responsible for the finite differences Δ in Table 3 emerge from application of the principle of corresponding states.[23] Deviations in reduced diffusion coefficients Δ_{ij} of hydrocarbon–hydrogen systems from a corresponding-states curve in which Δ_{ij} is plotted against $T/T_{c,12}$ are in the opposite sense to any deviation shown for H_2–H_2 self-diffusion for which quantum effects should be greatest owing to the small molecular masses. This result is found whether T_c and V_c of hydrogen are taken to be the experimental values or the effective critical constants used by Guggenheim and McGlashan [17] which correct in a semi-empirical way for quantum effects.

The Pidduck rough-sphere model [10] indicates the effect of interchange of translational and internal energy on the transport properties. On this model such enery transfer increases the apparent collision diameter for mass diffusion. This is in the sense shown with the more flexible hydrocarbons when hydrogen is the carrier gas. Present results strengthen the conclusion that the observed "hydrogen effects" indicate a greater efficiency for transferring energy to internal modes with hydrogen than with nitrogen; this ability is more pronounced with flexible than with inflexible hydrocarbons.

TABLE 3. *Calculated kinetic theory parameters σ_{22} for the systems studied* (Å).

	(H_2)	(D_2)	(He)	(N_2)	(A)	$\Delta = \sigma_{22}(H_2) - \sigma_{22}(N_2)$
			Rigid-sphere model			
n-Octane	7·33	7·06	6·83	6·94	7·44	+0·39
2 : 2 : 4-Trimethylpentane	7·07	6·97	6·73	7·02	7·33	+0·05
n-Heptane	7·23	6·84	6·54	6·91	6·92	+0·32
2 : 4-Dimethylpentane	7·00	6·71	6·57	6·88	6·94	+0·12
			Lennard-Jones 6 : 12 model			
n-Octane	7·26	7·15	7·23	6·25	6·68	+1·01
2 : 2 : 4-Trimethylpentane	7·12	7·04	7·22	6·61	6·77	+0·51
n-Heptane	7·52	7·13	7·17	6·81	6·73	+0·71
2 : 4-Dimethylpentane	7·21	6·94	7·16	6·69	6·66	+0·52

Comparisons between Hydrogen and Deuterium: Influence of Mass on "Roughness".— Comparisons involving these two molecules are particularly valuable since in collisions only mass, and not force-field, differences occur, to a first approximation. On either model, deuterium systematically yields smaller diameters than hydrogen (columns 2 and 3 of Table 3), indicating that it is less efficient in transferring energy to the internal degrees of freedom of the hydrocarbon, so that collisions are on average less rough. These differences are larger for the more flexible unbranched hydrocarbons, where "wrestling collisions" [16] might be expected to be more enveloping.

So far as results are available, ultrasonic methods of studying energy transfer yield the same general conclusions. In collisions leading to 0–1 vibrational quantum uptake

[16] McCoubrey, Parke, and Ubbelohde, *Proc. Roy. Soc.*, 1954, *A*, **223**, 155.
[17] Guggenheim and McGlashan, *ibid.*, 1951, *A*, **206**, 448.

in ethylene, deuterium is less efficient than hydrogen.[18] Deuterium is, however, more efficient than nitrogen.[18, 19]

Comparisons between deuterium and the nitrogen reference gas show somewhat different relative collision diameters in the present experiments according to which model is used (columns 3 and 5). This is because the less marked " hydrogen effect " with the isotopic deuterium is insufficient to outweigh other factors whose contribution in the two models differs. Such factors include molecular anisotropy and molecular attractive fields; but since the 6 : 12 model gives the more plausible sequence $H_2 > D_2 > N_2$ for the apparent collision diameters, contributions from the allowance for attractive force fields seem likely to account for the differences referred to.

These findings about the roughness of molecular collisions can be explained on the basis of the degree of approximation to adiabatic collisions in molecular encounters. Impact times will be shorter in collisions with hydrogen than with deuterium or nitrogen; short collisions tend to be less adiabatic and the probability of transfer of energy may be increased as a result.[20]

Influence of Rotational Quanta on Energy-transfer. Comparisons between Deuterium and Helium.—Alternatively to the above explanation, it has been suggested that the peculiar efficiency of the hydrogen molecule in effecting transfer of internal energy may be connected with the large magnitude of its rotational quanta;[21] the idea is that rotational degrees of freedom might absorb much of the excess of energy after vibrational deactivation. To illustrate this, Table 4 gives the magnitudes of the rotational quanta in terms of characteristic temperatures.[24]

TABLE 4. *Characteristic temperatures for rotation* (°K).

Molecule	H_2	D_2	N_2
$\theta_{rot.} = \frac{h^2}{8\pi^2 Ik}$	85·0	42·5	2·84

It is to be noted that both hydrogen and deuterium must change their rotational levels by several units of $k\theta_{rot.}$ at a time, unless spin isomerisation occurs during a collision. The vibrational quanta of hydrogen ($h\nu/k = 6140°$) and of deuterium ($h\nu/k = 4340°$) lie too high to contribute effectively in internal energy transfers.

In order to throw further light on the possible rôle of large rotational-energy quanta in permitting efficient transfer of internal energy, comparisons may be made between deuterium and helium (columns 3 and 4 of Table 3). The rigid-sphere model which makes no allowance for force fields or anisotropy factors gives $D_2 >$ He with no marked difference between branched and unbranched hydrocarbons. Allowance for force fields, but not for anisotropy, brings He $> D_2$ to an extent just outside probable error. It seems reasonable to conclude that the efficiencies of deuterium and of helium do not differ largely and that mass effects are considerably more important than any rotational-energy effects. On balance, ultrasonic measurements indicate that deuterium is more efficient than helium in converting translational into internal energy [19,22] of its collision partners, but further experiments seem desirable to test whether deuterium is uniformly somewhat more efficient than helium, by virtue of its rotational energy.

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[*Received, November 7th*, 1956.)

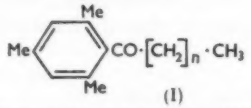
[18] Richards, *J. Chem. Phys.*, 1936, **4**, 561.
[19] Richards and Reid, *J. Chem. Phys.*, 1934, **2**, 206.
[20] Bethe and Teller, Aberdeen Proving Grounds, Ballistics Research Laboratory Report No. X-117, 1941; see also De Wette and Slawsky, *Physica*, 1954, **20**, 1169.
[21] Zener, *Phys. Rev.*, 1931, **37**, 556; cf. Oldenberg, *ibid.*, 1952, **87**, 786.
[22] Eucken and Jaacks, *Z. phys. Chem.*, 1935, **30**, *B*, 85; Petralia, *Nuovo cim.*, Suppl., 1952, **9**, 1; van Itterbeek and Mariens, *Physica*, 1940, **7**, 909.
[23] Rowlinson and Townley, *Trans. Faraday Soc.*, 1953, **49**, 20.
[24] Guggenheim, "Thermodynamics," North Holland Publ. Co., Amsterdam, 1949.

394. *The Formation of Oxothiomorpholides in the Willgerodt Reaction.*

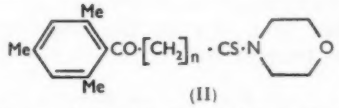
By P. A. Barrett.

From the Willgerodt reaction (sulphur–morpholine) with acetophenone, propiophenone, and their *p*-dimethylamino-derivatives the α-oxo-ω-thiomorpholides (VI), (XI), (XIV), and (XV) have been isolated, in addition to the orthodox Willgerodt thiomorpholides (V), (X), and (XIII). The formation of the oxothiomorpholides is favoured by the addition of nitrobenzene and suppressed by the presence of excess of hydrogen sulphide. They are however not appreciably reduced by hydrogen sulphide to the thiomorpholides, and are thus not shown to be intermediate in the formation of the latter. Their isolation does not necessitate revision of current theories on the mechanism of the Willgerodt reaction.

Dauben and Rogan [1] reported the isolation of the oxothiomorpholides (II; $n = 0$—2) on Willgerodt reaction with the mesityl ketones (I). They attributed formation of this new type of product to the weakly ketonic nature of mesityl ketones. Independently, we had isolated analogous oxothiomorpholides and shown that their formation is not limited to abnormal ketones.

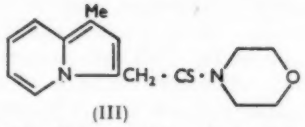


(I)

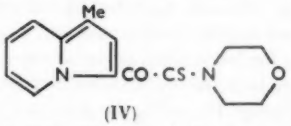


(II)

Our work had its origin in a Willgerodt reaction with 3-acetyl-1-methylpyrrocoline, from which was isolated in low yield, the orthodox product (III), and a compound to which on the basis of analysis and ultraviolet spectrum is assigned the constitution (IV). The method was therefore of little promise as a route to pyrrocolylacetic acids, but the isolation of the substituted thioglyoxylamide (IV), of a type then unknown as a product of Willgerodt reactions, suggested an examination of the behaviour of *p*-dimethylaminoacetophenone since reactivity of the 3-position in the pyrrocoline ring is similar to that of the *p*-position in dimethylaniline. Three compounds (V), (VI), and (VII) were then



(III)

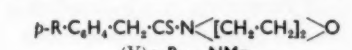


(IV)

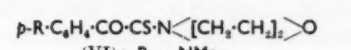
isolated. *p*-Dimethylaminophenylacet-thiomorpholide (V) was easily separated, through its greater basicity, from the scarlet mixture of (VI) and (VII), which formed mixed crystals but was separated by chromatography on alumina into yellow *p*-dimethylaminophenylglyoxylthiomorpholide (VI) and the intensely red *p*-dimethylaminophenyldithioglyoxylmorpholide (VII). The constitution of the product (VI) is confirmed by hydrolysis to *p*-dimethylaminophenylglyoxylic acid and by desulphurisation with silver acetate to *p*-dimethylaminophenylglyoxylmorpholide (VIII). The alternative structure (IX), not rigidly excluded by this evidence, is not only improbable on mechanistic grounds but is excluded by the ultraviolet absorption spectrum, discussed below. The constitution of the dithio-compound (VII) is confirmed by formation of this compound from the monothioanalogue (VI) by phosphorus pentasulphide. Re-examination of the Willgerodt reaction with acetophenone showed that the formation of oxothioamides is not abnormal. In addition to phenylacet-thiomorpholide [2] (X), there was isolated phenylglyoxylthiomorpholide (XI) which was shown (ultraviolet spectrum) to comprise 20% of the reaction

[1] Dauben and Rogan, *J. Amer. Chem. Soc.*, 1956, **78**, 4135.
[2] Schwenk and Bloch, *ibid.*, 1942, **64**, 3051.

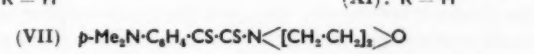
product: its constitution was confirmed by desulphurisation to phenylglyoxylmorpholide (XII), but its alkaline hydrolysis gave only mandelic acid. Lacking the tertiary amino-group, these products (X) and (XI) were not separable by the method used previously but differential hydrolysis with concentrated hydrochloric acid was a satisfactory method for the isolation of the oxo-amide (XI). The oxothiomorpholides (VI) and (XI) might have been intermediates in the formation of the thiomorpholides; in agreement, yields of



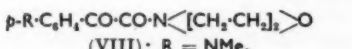
(V): R = NMe_2
(X): R = H



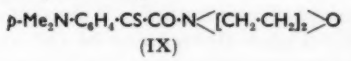
(VI): R = NMe_2
(XI): R = H



(VII)



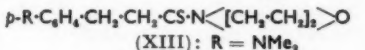
(VIII): R = NMe_2
(XII): R = H



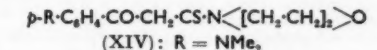
(IX)

the former were increased by the addition of an oxidising agent (nitrobenzene) to the reaction mixture (though they were not then the sole products), and were reduced virtually to zero when the reaction was carried out in a continuous current of hydrogen sulphide. That oxothioamides have not previously been isolated from Willgerodt reactions is probably related to variations in the reaction conditions used. The deficiency of hydrogen sulphide which favours their formation is more likely to be encountered in the sulphur–morpholine variant,[2] carried out in open vessels, than in the earlier methods[3] carried out under pressure.

p-Dimethylaminopropiophenone with sulphur and morpholine also gave two main products (XIII) and (XIV), with smaller amounts of *p*-dimethylaminocinnamthiomorpholide, and an unidentified compound $C_{11}H_{11}NS_3$. No analogue of the dithio-compound (VII) was isolated. The yield of the oxo-amide (XIV) was increased and no amide (XIII) could be isolated when nitrobenzene was added to the reaction mixture. The yield of the latter product (XIII) was increased and that of the former reduced by working in an atmosphere of hydrogen sulphide, but the course of the reaction was less completely influenced than in the case of the acetophenones.



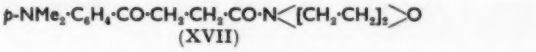
(XIII): R = NMe_2
(XVI): R = H



(XIV): R = NMe_2
(XV): R = H

The reaction of propiophenone with sulphur and morpholine has been used[4,5] for the preparation of β-phenylpropionic acid by hydrolysis of the total reaction product, but the intermediate thiomorpholide (XVI) has not been described. From the reaction was isolated in small yield a compound shown by analysis and ultraviolet spectrum to have the constitution (XV), but none could be isolated on reaction in the presence of nitrobenzene. The orthodox Willgerodt product (XVI) has not been isolated.

p-Dimethylaminobutyrophenone with sulphur and morpholine in the presence of nitrobenzene gave a compound (XVII). Its hypothetical thiomorpholide precursor presumably suffered hydrolysis during the working up.[6]



(XVII)

Although the formation of the oxothiomorpholides (VI), (XI), and (XIV) is substantially suppressed by excess of hydrogen sulphide, the oxothiomorpholides are not

[3] For refs. see Carmack and Spielman in "Organic Reactions," Vol. III, Chapman and Hall, London, 1946, p. 83.
[4] Schwenk and Papa, *J. Org. Chem.*, 1946, **11**, 798.
[5] McMillan and King, *J. Amer. Chem. Soc.*, 1948, **70**, 4148.
[6] Cf. Bernthsen, *Annalen*, 1877, **184**, 297.

XUM

themselves reduced by hydrogen sulphide in morpholine, but are recovered substantially unchanged. When heated in morpholine with sulphur and hydrogen sulphide, however, some reduction to the thiomorpholides occurs. An explanation of this difference in behaviour is suggested by the properties of the dithio-oxomorpholide (VII). This compound, unlike the accompanying oxothiomorpholide (VI), was rapidly converted by hydrogen sulphide into the thiomorpholide (V) [this is the preferred method for freeing the oxothiomorpholide (VI) from dithio-compound (VII)]. It is suggested that in the presence of sulphur the oxothiomorpholide (VI) slowly gives the thiomorpholide (V), *via* the dithio-compound (VII). The conversion of the oxothiomorpholides (VI), (XI), and (XIV) into the thiomorpholides (V), (X), and (XIII) by sulphur and hydrogen sulphide is however not sufficiently rapid for this to be the route by which the very high proportion of thiomorpholides is formed in Willgerodt reactions carried out in the presence of hydrogen sulphide. Unless the reaction of the oxothiomorpholides with sulphur and hydrogen sulphide in morpholine does not adequately reproduce the reducing conditions of the reaction mixture, isolation of the former does not afford evidence on the formation of the thiomorpholides, *i.e.*, on the mechanism of the Willgerodt reaction.

Ultraviolet Absorption Spectra (with Dr. A. J. EVERETT).—The ultraviolet absorption maxima of the compounds prepared are collected in the Table. The spectrum of phenyl-

Ultraviolet absorption spectra of thiomorpholides and related compounds.

	$\lambda_{max.}$ (mμ)		ε	
Acet-thiomorpholide	278		15,900	
Dimethyl-*p*-toluidine [a]	255,	303	34,700	2,240
Phenylacet-thiomorpholide (X)	282		15,650	
p-Dimethylaminophenylacet-thiomorpholide (V)	264, 279,	305 *	20,900, 19,100,	3,750
β-(*p*-Dimethylaminophenyl)propionthiomorpholide (XIII)	262, 279,	314 *	18,600, 17,700,	1,950
Acetophenone [b]	240,	278,† 320 †	13,000	1,100,
			50	
Phenylglyoxylthiomorpholide (XI)	254, 269,	376—384	17,850, 17,300,	1,020
Benzoylacet-thiomorpholide (XV)	244, 282,	320	11,350, 13,500,	6,530
Phenylglyoxylmorpholide (XII)	253,	285 *	14,000,	2,600
p-Dimethylaminoacetophenone	239,	334	6,600,	27,000
p-Dimethylaminophenylglyoxylthiomorpholide (VI)	264,	354	14,170,	27,000
p-Dimethylaminobenzoylacet-thiomorpholide (XIV)	243, 283,	340	7,120, 15,590,	27,400
β-(*p*-Dimethylaminobenzoyl)propionmorpholide (XVII)	237,	330	8,200,	33,300
p-Dimethylaminophenylglyoxylmorpholide (VIII)	243,	350	6,500,	28,700
p-Dimethylaminophenyldithioglyoxylmorpholide (VII)	246, 272,	458	8,550, 20,500,	47,700
Oxaldithiomorpholide	276		18,000	
1-Methylpyrrocoline [c]	239, 280, 288, 300,		33,000, 2,120,	3,150,
	360		4,350, 2,000	
(1-Methyl-3-pyrrocolyl)acet-thiomorpholide (III)	241, 281,	358—366	38,000, 18,000,	2,300
3-Acetyl-1-methylpyrrocoline	225, 229, 265, 370,		14,600, 13,100,	24,000,
	382		15,600, 14,300	
(1-Methyl-3-pyrrocolyl)glyoxylthiomorpholide (IV)	220, 227, 265, 398		12,500, 11,900,	25,000,
			20,000	
p-Dimethylaminocinnamthiomorpholide	236, 288—322,† 380		11,850, 18,750,	8,000
Substance $C_{11}H_{11}NS_2$	265, 325, 451		19,200, 6,300,	39,700

* Inflexion. † Fine structure.
[a] Remington, *J. Amer. Chem. Soc.*, 1945, **67**, 1838. [b] Braude, *Ann. Reports*, 1945, **42**, 105.
[c] Barrett, unpublished work.

acet-thiomorpholide (X) shows a single sharp peak at 282 mμ with rising end-absorption below 240 mμ, the absorption falling sharply to zero below 350 mμ; the spectrum is almost identical with that of acet-thiomorpholide [7] which has $\lambda_{max.}$ 278 mμ; it differs from the curve given by Dauben and Rogan [1] in lacking the shoulder at 365 mμ. This shoulder is however a feature of the spectrum of phenylglyoxylthiomorpholide (XI), which shows a

[7] Peak and Stansfield, *J.*, 1952, 4067.

broad peak at 360—385 mμ (ε 1020)—Dauben and Rogan's sample was probably contaminated with 20% of phenylglyoxylthiomorpholide. The spectra of dimethylaminophenyl-acet- and -propion-thiomorpholides (V and XIII) are almost identical, showing a broad double peak at 264 and 279 mμ, of which the former is attributed to the chromophore of dimethyl-*p*-toluidine and the latter to that of acet-thiomorpholide.

The spectra of α-(*p*-dimethylaminobenzoyl)acet-thiomorpholide (XIV) and β-(*p*-dimethylaminobenzoyl)propionmorpholide (XVII) agree in showing the two peaks at 240 and 340 mμ referable to *p*-dimethylaminoacetophenone. The former shows also the acet-thiomorpholide peak. The spectrum of benzoylacet-thiomorpholide (XV) shows a peak at 244 mμ referable to acetophenone, acet-thiomorpholide absorption at 282 mμ, and a shoulder at 320—322 mμ (ε 6530) which cannot be convincingly referred to either of these chromophores.

The substituted glyoxylthiomorpholides (IV), (VI), and (XI) are formally conjugated, and their spectra would not be expected to admit of the same clear interpretation in terms of constituent chromophores as the compounds considered above. However it appears that interaction between the groups is not sufficiently great to destroy the integrity of the absorption maxima associated with the individual chromophores, which survive, though in some cases with considerable alteration in wavelength. This is most clearly seen in the pyrrocolyl example (IV), whose spectrum very closely resembles that of the corresponding 3-acetylpyrrocoline except that the absorption maximum at 265 mμ is broadened towards 280 mμ, which is interpreted as a contribution from the thiomorpholide chromophore. Phenylglyoxylthiomorpholide (XI) shows a broad double peak at 254 and 269 mμ, of which the latter may represent the thiomorpholide chromophore, and the former peak together with the shoulder mentioned above, may be referred to the acetophenone chromophore, both contributions having suffered considerable modification. The dimethylamino-analogue (VI) shows a survival of two absorption maxima, of which that at 264 mμ may represent a fusion of the shorter-wavelength acetophenone peak with the thiomorpholide contribution, and that at 354 mμ may be referred to dimethylaminoacetophenone. The spectra of phenylglyoxylmorpholide (XII) and its dimethylamino-analogue (VIII) are less confused. The morpholide group appears to show neither contribution to, nor influence on, the spectra, which respectively resemble rather closely those of acetophenone and dimethylaminoacetophenone. Similarly the spectrum of oxaldithiomorpholide [8] shows no evidence of interaction between the two thioamide groups, the maximum being identical with that of, *e.g.*, acet-thiomorpholide.

A similar absence of interaction being assumed for the dithioglyoxylmorpholide (VII), its absorption maximum at 272 mμ (ε 20,500) is attributed to the thiomorpholide chromophore, and the maxima at 246 and 458 mμ are referred to the dimethylaminothioacetophenone chromophore. The absence of the 458 mμ maximum from the spectra of the monothioglyoxylmorpholides (*e.g.*, VI and XI) shows that the sulphur atom is always in the β- and not the α-position.

Experimental

Ultraviolet absorption spectra were measured in ethanol in a Hilger "Uvispek" spectrophotometer.

Willgerodt Reactions.—(a) *3-Acetyl-1-methylpyrrocoline.* A mixture of 3-acetyl-1-methylpyrrocoline [9] (18 g.), sulphur (5·5 g.), and morpholine (15 ml.) was boiled under reflux for 21 hr., then extracted with boiling ether (1·5 l. in portions). The extracts were decanted from tar, and the ether removed. The oil was washed with water to remove morpholine and the residual semisolid material was crystallised from ethanol, to give (*1-methyl-3-pyrrocolyl)glyoxylthiomorpholide* (IV) (2·5 g.), as orange needles, m. p. 192° (Found: C, 62·6; H, 5·6; O, 11·5; N, 9·3; S, 10·6. $C_{15}H_{16}O_2N_2S$ requires C, 62·5; H, 5·6; O, 11·1; N, 9·7; S, 11·1%). (It is

[8] King and McMillan, *J. Amer. Chem. Soc.*, 1947, **69**, 1207.
[9] B.P. Appl. 35,513/1953.

probable that much of this material was discarded in the ether-insoluble tar.) The mother-liquors were evaporated to give semisolid material from which by crystallisation from light petroleum (b. p. 60—80°), in which the glyoxylthiomorpholide is sparingly soluble, was isolated (*1-methyl-3-pyrrocolyl*)*acet-thiomorpholide* (III) (0·6 g.) as cream-coloured needles, m. p. 130° (Found: C, 65·7; H, 6·4; O, 6·2; N, 9·5; S, 11·8. $C_{15}H_{18}ON_2S$ requires C, 65·7; H, 6·6; O, 5·8; N, 10·2; S, 11·7%).

(b) *Acetophenone.* (i) Following Schwenk and Bloch,[9] acetophenone (12 ml.), sulphur (4·8 g.), and morpholine (9·0 ml.) were boiled under reflux for 8 hr. On cooling, the mixture deposited crystals which were lixiviated with water, and the solid (12 g.) was filtered off and recrystallised several times from ethanol to give phenylacet-thiomorpholide (X), colourless prisms (7·5 g., 34%), m. p. 79—80° (Schwenk and Bloch [9] give m. p. 79—80°). From the filtrate, by evaporation, was obtained a mixture of colourless and yellow crystals from which by hand-picking of the yellow and recrystallisation from ethanol was obtained a small sample of phenylglyoxylthiomorpholide (XI), m. p. 113°, not depressed on admixture with material prepared as described below.

The total product from a second experiment, after one crystallisation from ethanol (10 g.), was shown by a comparison of its ultraviolet spectrum with that of the pure components to contain 20·8% of the glyoxylthiomorpholide.

(ii) With addition of nitrobenzene. Acetophenone (120 ml.), sulphur (48 g.), morpholine (180 ml.), and nitrobenzene (120 ml.) were boiled under reflux for 4 hr. The product was washed free from morpholine by water (3 × 1 l.), and the oil steam-distilled. The aqueous layer was poured off and to the semisolid residue was added a mixture of concentrated hydrochloric acid (630 ml.) and acetic acid (630 ml.). The mixture was boiled under reflux for 2 hr., poured on ice, and basified by aqueous ammonia. The solid was filtered off, washed with water, dried *in vacuo*, and recrystallised from ethanol to give *phenylglyoxylthiomorpholide* (XI) (65 g., 28%) as yellow plates, m. p. 114° (Found: C, 61·4; H, 5·4; O, 14·5; S, 13·7. $C_{12}H_{13}O_2NS$ requires C, 61·4; H, 5·5; O, 13·6; S, 13·6%).

(iii) In presence of excess of hydrogen sulphide. Acetophenone (48 ml.), sulphur (19·2 g.), and morpholine (54 ml.) were boiled under reflux for 4 hr. in a current of hydrogen sulphide. Working up as described under (i) gave phenylacet-thiomorpholide (67 g., 76%). From the residue obtained by evaporation of the filtrates from the crystallisations there was obtained, by the hydrolysis method described under (ii), phenylglyoxylthiomorpholide (2·5 g.), m. p. 112—113°.

(c) p-*Dimethylaminoacetophenone.* (i) *p*-Dimethylaminoacetophenone [10] (32·6 g.), sulphur (9·6 g.), and morpholine (26·0 ml.) were boiled under reflux for 4 hr. The product solidified on cooling. It was recrystallised from ethanol to give solid (38 g.). This was dissolved in warm acetic acid (175 ml.), the solution filtered, and diluted with water (200 ml.). Scarlet crystals rapidly separated and after ½ hr. were filtered off, washed with a little 50% aqueous acetic acid and then with water, and crystallised from ethanol, to give a mixture of the mono- and di-thioglyoxylmorpholide (VI and VII) as red plates (8·3 g.), m. p. 159—162° (Found: C, 59·3; H, 6·0; S, 13·8%). The aqueous acetic acid filtrate was basified with ammonia solution with cooling. The precipitated, almost colourless, solid was filtered off, washed with water, and recrystallised from ethanol, to give p-*dimethylaminophenylacet-thiomorpholide* (V) (25·2 g.) as colourless, serrated prisms, m. p. 140—142° (Found: C, 64·0; H, 7·2; O, 6·4; N, 10·3; S, 11·9. $C_{14}H_{20}ON_2S$ requires C, 63·6; H, 7·6; O, 6·1; N, 10·6; S, 12·1%). 5 g. of mixed mono- and di-thioglyoxylmorpholides were dissolved in benzene (50 ml.) and adsorbed on alumina (450 g.; 4 × 40 cm.). Elution with benzene developed an orange head band and a yellow tail band without effecting their complete separation. The orange band was eluted and adsorbed on a second column. Development gave discrete orange and yellow bands. The orange band was eluted, and after removal of the solvent gave deep crimson solid. Crystallisation from ethanol gave p-*dimethylaminophenyldithioglyoxylmorpholide* (VII) (0·5 g.), deep red needles with a metallic reflex, m. p. 200° (Found: C, 57·6; H, 6·3; N, 9·5; S, 21·4. $C_{14}H_{18}ON_2S_2$ requires C, 57·1; H, 6·1; N, 9·5; S, 21·8%). The yellow bands were stripped with chloroform and the eluate on evaporation and crystallisation from ethanol gave *p*-dimethylaminophenylglyoxylthiomorpholide (see below) (2·2 g.; m. p. 153—154°) contaminated with low-melting material presumably formed by decomposition on the column. For the preparation of pure

[10] Nineham, *J.*, 1952, 635.

monothioglyoxylmorpholide the following method is preferred. Mixed mono- and di-thioglyoxylmorpholides (14·0 g.) (prepared as described above) were boiled under reflux in morpholine (20 ml.) while a current of hydrogen sulphide was passed for 5 min. The product was cooled somewhat and diluted with ethanol (30 ml.). Pale yellow crystalline material separated and was filtered off and dried. Recrystallisation from ethanol gave p-*dimethylaminophenylglyoxylthiomorpholide* (VI) (11·0 g.) as pale yellow prisms, m. p. 161—162° (Found: C, 60·8; H, 6·2; O, 11·6; N, 10·3; S, 11·3. $C_{14}H_{18}O_2N_2S$ requires C, 60·4; H, 6·5; O, 11·5; N, 10·1; S, 11·5%). The filtrates from the crystallisations were taken to dryness and the residue, consisting of a mixture of *p*-dimethylaminophenyl-acet- and -glyoxyl-thiomorpholides, was separated by the acetic acid method described above, to give *p*-dimethylaminophenylacet-thiomorpholide (0·8 g.), m. p. 141—142°.

(ii) With addition of nitrobenzene. *p*-Dimethylaminoacetophenone (163 g.), sulphur (96 g.), morpholine (174 ml.), and nitrobenzene (124 ml.) were boiled under reflux for 4 hr. The product, while still warm, was diluted with an equal volume of ethanol and set aside for 48 hr. The red crystals (251 g.) were filtered off, washed with ethanol, dissolved in glacial acetic acid (2 l.) at *ca.* 80°, the solution filtered from sulphur, and left for 48 hr. The mixed thioglyoxylmorpholides (83 g.) were filtered off and washed with glacial acetic acid. The acid filtrate was diluted with water (2 l.) and left for 6 hr. The second crop of mixed thioglyoxylmorpholides (36 g.) was filtered off and washed with 50% aqueous acetic acid. The aqueous acid filtrate was cautiously basified (ammonia) at 0°. The precipitated solid (106 g.), consisting of *p*-dimethylaminophenylacet-thiomorpholide still containing thioglyoxylmorpholides, was dissolved in glacial acetic acid (400 ml.), diluted with water (500 ml.), and left for 1 hr. The third crop of mixed thioglyoxylmorpholides (10 g.) was filtered off. The combined crops of crude material (129 g.) were crystallised from ethanol (*ca.* 4 l.), to give mixed mono- and di-thio-glyoxylthiomorpholides as red plates (115 g.), m. p. 160—161°. These were boiled under reflux in morpholine (115 ml.) while a current of hydrogen sulphide was passed for 10 min. The solution was cooled somewhat, diluted with an equal volume of ethanol, and left 6 hr. The pale yellow solid was filtered off, washed with ethanol, and dried at 60° (104 g.; m. p. 151—152°). Crystallisation from ethanol gave *p*-dimethylaminophenylglyoxylthiomorpholide (98 g.), m. p. 161—162°.

The second aqueous acetic acid filtrate was worked up as described above, to give *p*-dimethylaminophenylacet-thiomorpholide (38 g.), m. p. 139—140°.

(iii) In the presence of excess of hydrogen sulphide. *p*-Dimethylaminoacetophenone (16·3 g.), sulphur (3·2 g.), and morpholine (18 ml.) were boiled under reflux for 4 hr. while a slow stream of hydrogen sulphide was bubbled through. The mixture was cooled, diluted with a little ethanol, and left overnight. The solid (20 g.) was filtered off, washed with ethanol, and dissolved in water by addition of 2N-hydrochloric acid. The aqueous solution was filtered from sulphur, treated with charcoal (2 g.), refiltered, and basified with ammonia at 0°, and the precipitated solid was filtered off, washed, and dried *in vacuo*. Several recrystallisations from ethanol to free the material from a trace of bright yellow impurity gave *p*-dimethylaminophenylacet-thiomorpholide (16 g.) as colourless prisms. No glyoxylthiomorpholide could be found in the filtrates from the ethanol crystallisation. *p*-Dimethylaminophenylglyoxylthiomorpholide (1·2 g.), m. p. 156°, was however recovered by working up the original reaction filtrate.

(d) *Propiophenone.* Propiophenone (13·0 ml.), sulphur (9·6 g.), and morpholine (18·0 ml.) were boiled under reflux for 7 hr. After cooling, the product was washed with water to remove morpholine, and the residual dark oil was extracted several times with ether. The ether solution was decanted from brown tar, filtered (charcoal), and evaporated to give a brown oil. After several days this deposited crystals. The semi-solid mass was lixiviated with ethanol and filtered to give an almost colourless solid (3·0 g.). Crystallisation from ethanol gave *benzoylacet-thiomorpholide* (XV) as almost colourless prisms, m. p. 129—130° (Found: C, 62·9; H, 6·1; O, 13·4; S, 13·2. $C_{12}H_{15}O_2NS$ requires C, 62·6; H, 6·1; O, 12·9; S, 12·9%).

(e) p-*Dimethylaminopropiophenone.* (i) *p*-Dimethylaminopropiophenone [10] (35·4 g.), sulphur (19·2 g.), and morpholine (36 ml.) were boiled under reflux for 13 hr., cooled somewhat, diluted with an equal volume of ethanol, and left overnight. The solid was filtered off, washed with a little ethanol, recrystallised from a small volume of ethanol, and suspended in water (400 ml.), and 2N-hydrochloric acid was added cautiously with stirring until the bright yellow finely divided material was dissolved, leaving brownish crystals undissolved. This solid was

filtered off, washed with water, and after several crystallisations from ethanol (charcoal) gave p-*dimethylaminobenzoylacet-thiomorpholide* (XIV) (16 g.) as almost colourless needles, m. p. 156° (Found: C, 61·6; H, 6·9; O, 10·9; S, 10·8. $C_{15}H_{20}O_2N_2S$ requires C, 61·6; H, 6·9; O, 11·0; S, 11·0%). The aqueous filtrate was basified (ammonia) at 0°. The yellow precipitate was filtered off, washed with water, dried *in vacuo*, dissolved in glacial acetic acid (100 ml.), and diluted with water (350 ml.). After 1 hr., the bright yellow precipitate was filtered off and recrystallised from ethanol to give p-*dimethylaminocinnamthiomorpholide* (1·5 g.) as deep yellow plates, m. p. 170° (Found: C, 65·0; H, 6·9; N, 10·4; S, 11·3. $C_{15}H_{20}ON_2S$ requires C, 65·1; H, 7·3; N, 10·2; S, 11·6%). The aqueous acetic acid filtrate was further diluted with water (800 ml.), charcoal (2 g.) was added, and after ¼ hr. the solution was filtered and basified (ammonia) and the almost colourless precipitate was filtered off, washed with water, dried *in vacuo* (11·5 g.), and recrystallised from a small volume of ethanol to give β-p-*dimethylaminophenylpropionthiomorpholide* (XIII) as colourless needles, m. p. 117° (Found: C, 64·6; H, 7·9; N, 10·3; S, 11·3. $C_{15}H_{22}ON_2S$ requires C, 64·8; H, 7·9; N, 10·1; S, 11·5%).

(ii) With addition of nitrobenzene. *p*-Dimethylaminopropiophenone (35·4 g.), sulphur (19·2 g.), morpholine (36·0 ml.), and nitrobenzene (30·0 ml.) were boiled under reflux for 17 hr. While still warm the mixture was diluted with an equal volume of ethanol. After being kept overnight, the resulting solid was filtered off, washed with ethanol, and recrystallised from ethanol (*ca.* 2 l.) to give *p*-dimethylaminobenzoylacet-thiomorpholide (36 g.) as pale orange needles, m. p. 152—154°. Further crystallisation raised the m. p. to 155—156° but did not entirely remove the orange colour. The filtrate from the first ethanol crystallisation was taken down to dryness, and the residual solid (5 g.), a mixture of the benzoylacet-thiomorpholide, sulphur, and a dark red substance, was freed from the first by warming it to *ca.* 80° with excess of 2N-hydrochloric acid in which the thiomorpholide is soluble. The material insoluble in 2N-hydrochloric acid was filtered off and washed with a few ml. of carbon disulphide to free it from sulphur. The residual dark red material (0·5 g.) was recrystallised from ethanol to give a *substance* as reddish-purple needles, m. p. 208° (Found: C, 52·1; H, 4·2; O, 0; N, 5·5; S, 37·9. $C_{11}H_{11}NS_3$ requires C, 52·2; H, 4·4; N, 5·5; S, 38·0%).

(iii) In presence of excess of hydrogen sulphide. *p*-Dimethylaminopropiophenone (35·4.), sulphur (19·2 g.), and morpholine (36 ml.) were boiled under reflux for 7 hr., while a slow stream of hydrogen sulphide was passed through. Working up as described under (i) gave *p*-dimethylaminobenzoylacet-thiomorpholide (11 g.), *p*-dimethylaminocinnamthiomorpholide (3·8 g.) and β-*p*-dimethylaminophenylpropiothiomorpholide (19·6 g.).

(f) p-*Dimethylaminobutyrophenone*. *p*-Dimethylaminobutyrophenone [10] (38·2 g.), sulphur (9·6 g.), morpholine (36·0 ml.), and nitrobenzene (240 ml.) were boiled under reflux for 6 hr. The dark product was steam-distilled; the residual oil partially solidified after several days. The black semi-solid mass was lixiviated with acetone and filtered. The discoloured fawn solid (20 g.) was washed cautiously with acetone and with ethanol, and crystallised (charcoal) from ethanol to give β-p-*dimethylaminobenzoylpropionmorpholide* (XVII) (17 g.) as straw-coloured prisms, m. p. 169° (Found: C, 66·7; H, 7·7; O, 16·6; N, 9·4; S, 0. $C_{16}H_{22}O_3N_2$ requires C, 66·2; H, 7·6; O, 16·6; N, 9·7%).

Behaviour of Phenylglyoxylthiomorpholide towards Hydrogen Sulphide.—Phenylglyoxylthiomorpholide (10 g.) and morpholine (10 ml.) were boiled under reflux for 4 hr., while a slow current of hydrogen sulphide was passed through. After cooling, the yellow mixture was diluted with water. The oil which separated immediately solidified and was filtered off, washed, and dried *in vacuo*. The crude product had m. p. 103—105°. Crystallisation from ethanol gave recovered phenylglyoxylthiomorpholide (8·5 g.), m. p. and mixed m. p. 114°.

Reaction of Phenylglyoxylthiomorpholide with Sulphur and Hydrogen Sulphide.—Phenylglyoxylthiomorpholide (20 g.), sulphur (1·6 g.), and morpholine (10 ml.) were boiled under reflux for 4 hr. while a slow current of hydrogen sulphide was passed through. The product was cooled and washed with water to remove morpholine. The residual dark oil was dissolved in a little ethanol and left overnight. The brown crystals (15 g.) were filtered off and washed with ethanol. Further crystallisations from ethanol (charcoal) gave recovered phenylglyoxylthiomorpholide (4 g.; m. p. 112—113°) and pale yellow crystalline material (7·5 g.) shown by ultraviolet spectrum to contain 29·6% of phenylglyoxylthiomorpholide. From it by fractional crystallisation there was obtained colourless phenylacet-thiomorpholide (3·4 g.), m. p. and mixed m. p. 77—79°.

Behaviour of p-*Dimethylaminophenylglyoxylthiomorpholide towards Sulphur and Hydrogen*

Sulphide.—*p*-Dimethylaminophenylglyoxylthiomorpholide (10 g.), sulphur (1·5 g.), and morpholine (6·0 ml.) were boiled under reflux for 4 hr. while a slow current of hydrogen sulphide was passed through. After cooling, the mixture was diluted with an equal volume of ethanol. The solid was filtered off and separated by the acetic acid method (see above) to give recovered glyoxylthiomorpholide (6·0 g.; m. p. and mixed m. p. 157—159°) and *p*-dimethylaminophenylacet-thiomorpholide (1·2 g.; m. p. and mixed m. p. 139—140°).

Behaviour of p-*Dimethylaminobenzoylacet-thiomorpholide towards Sulphur and Hydrogen Sulphide.*—*p*-Dimethylaminobenzoylacet-thiomorpholide (15 g.), sulphur (1·6 g.), and morpholine (10 ml.) were boiled under reflux for 5 hr. while a current of hydrogen sulphide was passed. The product, recrystallised from ethanol, gave recovered benzoylacet-thiomorpholide (9·0 g.; m. p. 153—154°). The ethanol filtrates were taken down to dryness. The dark residue was washed with water and dissolved in glacial acetic acid (25 ml.), the solution was diluted with water (200 ml.) and filtered twice (charcoal) to remove tar, and the filtrate was neutralised with ammonia. The precipitated solid (0·5 g.) was filtered off, washed with water and recrystallised from ethanol to give β-*p*-dimethylaminophenylpropiothiomorpholide (0·2 g.), m. p. and mixed m. p. 115—116°.

p-*Dimethylaminophenyldithioglyoxylmorpholide* (VII) *from the Monothiomorpholide* (VI).—The monothiomorpholide (2·7 g.), phosphorus pentasulphide (3·0 g.), and dry benzene (50 ml.) were boiled under reflux for ½ hr. The deep red solution was filtered from insoluble matter and evaporated to dryness. The dark red residue was recrystallised twice from ethanol, to give *p*-dimethylaminophenyldithioglyoxylmorpholide (0·6 g.), m. p. and mixed m. p. 196—197° (Found: S, 20·65%).

Hydrolysis of p-*Dimethylaminophenylglyoxylthiomorpholide to* p-*Dimethylaminophenylglyoxylic Acid.*—*p*-Dimethylaminophenylglyoxylthiomorpholide (5·56 g.), potassium hydroxide (1·12 g.) in water (2 ml.), and ethanol (50 ml.) were boiled under reflux for 1½ hr. The ethanol was removed *in vacuo* and the residue stirred with water and filtered. The solid was dried *in vacuo* (4·3 g.). It was expected that this would be substantially *p*-dimethylaminophenylglyoxylmorpholide (VIII) but crystallisation from ethanol gave yellow material (3·1 g.), m. p. 120—130°, containing 4·8% of S. It was boiled with potassium hydroxide (2·24 g.) in water (3 ml.) and ethanol (50 ml.) for 4 hr. On cooling, colourless plates (1·4 g.) separated. These were filtered off and recrystallised from ethanol, to give *potassium* p-*dimethylaminophenylglyoxylate*, m. p. 300° (Found: C, 51·3; H, 4·6; N, 6·1. $C_{10}H_{10}O_3NK$ requires C, 52·0; H, 4·3; N, 6·1%). It was dissolved in a little water and just acidified by acetic acid. *p*-Dimethylaminophenylglyoxylic acid separated as golden-yellow plates, which after crystallisation from ethanol had m. p. 185—186°, not depressed on admixture with an authentic specimen prepared by Staudinger's method.[11]

p-*Dimethylaminophenylglyoxylmorpholide.*—The thiomorpholide (2·78 g.), silver acetate (3·34 g.), water (5 ml.), and ethanol (50 ml.) were boiled under reflux for 1½ hr. The precipitated silver sulphide was filtered off and the pale yellow filtrate evaporated to dryness. The residue was stirred with water, and the solid was filtered off, dried in the air (2 g.), and recrystallised from a small volume of ethanol, to give p-*dimethylaminophenylglyoxylmorpholide* (VIII) as almost colourless needles, m. p. 140° (Found: C, 63·9; H, 6·9; N, 10·7; O, 18·4. $C_{14}H_{18}O_3N_2$ requires C, 64·1; H, 6·9; N, 10·7; O, 18·3%).

Hydrolysis of Phenylglyoxylthiomorpholide.—Phenylglyoxylthiomorpholide (5·7 g.), potassium hydroxide (6·7 g.) in water (5 ml.), and ethanol (50 ml.) were boiled under reflux for 4 hr. The ethanol was removed by distillation and the residue dissolved in a little water, acidified with hydrochloric acid, and extracted thrice with ether. The ether extracts were dried (Na_2SO_4) and filtered (charcoal) and the ether was distilled off to leave an oil (3·2 g.) which rapidly solidified and after crystallisation from carbon tetrachloride gave mandelic acid (0·9 g.) as colourless plates, m. p. and mixed m. p. 115—116·5° (Found: C, 63·0; H, 5·2; N, 0. Calc. for $C_8H_8O_3$: C, 63·5; H, 5·3%).

Phenylglyoxylmorpholide.—Phenylglyoxylthiomorpholide (5·9 g.), silver nitrate (8·5 g.) in water (10 ml.), and ethanol (125 ml.) were boiled under reflux for ½ hr. The precipitated silver sulphide was filtered off and the filtrate was evaporated to dryness, diluted with water, and extracted twice with ether. The ether extracts were dried (Na_2SO_4) and evaporated to give an oil (4·3 g.) which slowly solidified and was recrystallised from a large volume of light petroleum

[11] Staudinger, *Ber.*, 1909, **42**, 3489.

XUM

(b. p. 60—80°) to give *phenylglyoxylmorpholide* (XII) as colourless needles, m. p. 50—51° (Found: C, 66·3; H, 6·0; O, 21·3; N, 6·4. $C_{12}H_{13}O_3N$ requires C, 65·8; H, 5·9; O, 21·9; N, 6·4%).

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395. *Studies of* Aspergillus niger. *Part V.* The Enzymic Synthesis of a New Trisaccharide.*

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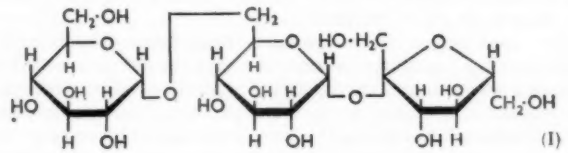
A trisaccharide produced by the action of *A. niger* "152" on a sucrose–maltose mixture has been characterised as *O*-α-D-glucopyranosyl-(1 ⟶ 6)-*O*-α-D-glucopyranosyl-(1 ⟶ 2) β-D-fructofuranoside.

IN a search for possible precursors of nigeran, the polysaccharide synthesised [1] by *Aspergillus niger* "152", the action of a cell-free extract of the mould on a mixture of sucrose and maltose was examined. From the complex mixture of oligosaccharides produced, we isolated a new trisaccharide (X), the structure of which we now report.

The mixture was separated by fractionation on a charcoal column [2] with successively smaller gradients of aqueous ethanol. The main trisaccharides produced were crystalline panose, a ketose that behaved on a paper chromatogram in the same way as *O*-α-D-glucopyranosyl-(1 ⟶ 2)-*O*-β-D-fructofuranosyl-(1 ⟶ 2) β-D-fructofuranoside, and trisaccharide X. The first two presumably arose by transglucosidation from maltose and transfructosidation from sucrose, respectively.[3]

Trisaccharide X was rapidly hydrolysed by 0·1N-hydrochloric acid at 100° to *iso*-maltose (isolated as β-*iso*maltose octa-acetate) and fructose. The observed optical rotation, $[\alpha]_D^{18}$ +46·7°, was in good agreement with that (+48·4°) calculated on the same basis for an equimolar mixture of *iso*maltose (+120°) and fructose (−92·4°) and the molar ratio aldobiose : ketose determined by Van der Plank's method [4] was 0·87 : 1. Since trisaccharide X was non-reducing and showed a low mobility on borate-buffer ionophoresis, this evidence and the conditions of its synthesis suggested that it was *O*-α-D-glucopyranosyl-



(I)

(1 ⟶ 6)-*O*-α-D-glucopyranosyl-(1 ⟶ 2) β-D-fructofuranoside (I). As would be expected, its optical rotation ($[\alpha]_D^{18}$ +102·5°) was slightly smaller than that of raffinose pentahydrate ($[\alpha]_D^{20}$ +105·2°) [cf. melibiose, +129·5° (equil.); *iso*maltose, +120° (equil.)]. Its infrared

* Part IV, *J.*, 1955, 3734.

[1] Barker, Bourne, and Stacey, *J.*, 1953, 3084.
[2] Whistler and Durso, *J. Amer. Chem. Soc.*, 1950, **72**, 677.
[3] Barker and Carrington, *J.*, 1953, 3588; Barker, Bourne, and Carrington, *J.*, 1954, 2125.
[4] Van der Plank, *Biochem. J.*, 1936, **30**, 460.

spectrum was almost a summation of those of *iso*maltose and sucrose and showed a certain similarity to that of raffinose :

Trisaccharide X ...		919s			870m	852m	835m	803vw	769m
*iso*Maltose		919s					838m		768m
Sucrose	942m	919s	907s		865m	846m		797vw	
Raffinose	938s			888vw	872m	857m	830s		770m

Trisaccharide X should give, on periodate oxidation, the same hexa-aldehyde as raffinose [*O*-α-D-galactopyranosyl-(1 → 6)-*O*-α-D-glucopyranosyl-(1 → 2) β-D-fructofuranoside]. After treatment of trisaccharide X and of raffinose with periodate, the observed final optical rotations (+46·0°, + 48·2°), the formic acid produced (1·7, 1·9 mol.), and the periodate consumed (5·1, 5·2 mol.) were very similar.[5]

When the trisaccharide was methylated and then hydrolysed, paper chromatography showed the presence of 2 : 3 : 4-tri-*O*- and 2 : 3 : 4 : 6-tetra-*O*-methylglucose, a tetra-*O*-methylfructose, and traces of other products formed by incomplete methylation. This confirms the assigned structure.

The structure of trisaccharide X makes it probable that it was synthesised by the transglucosidase mentioned above, acting on maltose as substrate and using sucrose as receptor. Such a trisaccharide might be a possible intermediate in the synthesis of dextran from sucrose. White and Maher [6] isolated an analogue [*O*-α-D-glucopyranosyl-(1 → 4)-*O*-α-D-glucopyranosyl-(1 → 2) β-D-fructofuranoside] after treating sucrose with honey invertase.

Experimental

Enzymic Synthesis of Oligosaccharide Mixture (with T. R. Carrington).—A freeze-dried cell-free extract [3] (5 g.) of *Aspergillus niger* " 152 ", dissolved in sterile distilled water (100 c.c.), was mixed with an aqueous sterile solution (300 c.c.) of maltose hydrate (50 g.) and sucrose (50 g.). After 70 hr. at 30° $[\alpha]_D^{17}$ had fallen to *ca.* +46·6° (*c* 5 in H_2O) and paper chromatography with the organic phase of butanol–ethanol–water–ammonia (40 : 10 : 49 : 1) revealed components having R_F values identical with those of fructose, glucose, sucrose, maltose, *O*-α-D-glucopyranosyl-(1 → 2)-*O*-β-D-fructofuranosyl-(1 → 2) β-D-fructofuranoside, panose, an unknown trisaccharide (X), and higher oligosaccharides. After adjustment of the pH to 7·2, enzyme action was arrested by 15 minutes' heating at 100°. After fractionation on a charcoal column [3] with gradient elution with aqueous ethanol,[7] the monosaccharides and most of the disaccharides (76·62 g.) were discarded. The trisaccharides were obtained in two fractions : A (10·69 g.), a mixture of maltose, *O*-α-D-glucopyranosyl-(1 → 2)-*O*-β-D-fructofuranosyl-(1 → 2) β-D-fructofuranoside, trisaccharide X, and panose; and B (5·05 g.) which contained the same sugars together with higher oligosaccharides.

Isolation of Trisaccharide X.—Fraction A was refractionated on a charcoal column (65 × 4·6 cm. diam.) with gradient elution with 5—30% ethanol (8 l.), and freed from maltose and most of the *O*-α-D-glucopyranosyl-(1 → 2)-*O*-β-D-fructofuranosyl-(1 → 2) β-D-fructofuranoside. The enriched fraction was freeze-dried to a powder (5·79 g.). The trisaccharides were extracted with boiling methanol (200 c.c.), and the solution set aside for 4 days at room temperature. Two crops (1·82 g.; 0·25 g.) of crystals (panose) were obtained, and the remaining trisaccharide mixture (3·68 g.) was refractionated on the charcoal column used above but with a lower gradient (5—15% ethanol; 8 l.). One fraction containing chromatographically pure trisaccharide X (0·225 g.) was obtained. The remaining fractions, when separated on a smaller charcoal column (39 × 2·5 cm. diam.) with a very small gradient (8·5—11% ethanol; 3 l.) afforded further pure trisaccharide X (0·476 g.) and a mixed fraction (0·273 g.) of panose and trisaccharide X.

Characterisation of Trisaccharide X.—(i) *Paper chromatography and ionophoresis.* In the solvent mixture described above, trisaccharide X moved as a single component (R_G 0·26) on a

[5] Cf. Hérissey, Wickstrom, and Courtois, *Bull. Soc. Chim. biol.*, 1951, **33**, 1768.
[6] White and Maher, *J. Amer. Chem. Soc.*, 1953, **75**, 1259.
[7] Alm, Williams, and Tiselius, *Acta Chem. Scand.*, 1952, **6**, 826.

paper chromatogram. The corresponding values for panose and *O*-α-D-glucopyranosyl-(1 ⟶ 2)-*O*-β-D-fructofuranosyl-(1 ⟶ 2) β-D-fructofuranoside, were R_G 0·21 and R_G 0·34, respectively. The relative times needed for spots containing equal quantities of the three trisaccharides to develop their full intensity when sprayed with alkaline silver nitrate [8] were panose ≪ *O*-α-D-glucopyranosyl-(1 ⟶ 2)-*O*-β-D-fructofuranosyl-(1 ⟶ 2) β-D-fructofuranoside < trisaccharide X. On paper ionophoresis in borate buffer,[9] pH 10, the mobility of trisaccharide X was M_G 0·04 and that of panose M_G 0·19.

(ii) *Optical measurements.* Amorphous trisaccharide X showed $[\alpha]_D^{18}$ +102·5° (*c* 2 in H_2O). A small amount of trisaccharide X was crystallised from ethanol and had m. p. 118—120°. The infrared spectrum of the crystalline material in the region 1027—715 cm.$^{-1}$ showed absorption peaks at 978s, 919s, 870m 852m, 835m, 803vw, 769m cm.$^{-1}$.

(iii) *Partial acidic hydrolysis.* Trisaccharide X (57·8 mg.) was hydrolysed with 0·1N-hydrochloric acid (6 c.c.) at 100°. After 5 min. $[\alpha]_D^{18}$ had fallen from +102·5° to +46·7° and thereafter was constant for a further 5 min. The only components detectable by paper chromatography and ionophoresis were those having the same mobilities as fructose and *iso*maltose, together with traces of glucose and trisaccharide X. Quantitative determination [4] of the proportion of aldobiose to keto-sugar (approx. equal to the *iso*maltose : fructose ratio) in the partial hydrolysate after 7 min. gave a molar ratio 0·87 : 1. Further hydrolysis at 100°, after increase of the concentration of hydrochloric acid to N, hydrolysed the disaccharide, and only glucose and fructose were present in the final hydrolysate.

(iv) *Isolation of the products of partial hydrolysis.* Trisaccharide X (219 mg.) was hydrolysed with 0·1N-hydrochloric acid at 100° for 7 min. After neutralisation with silver carbonate, filtration, and concentration *in vacuo*, the products were fractionated on a charcoal–"Celite" column (40 × 2·5 cm. diam.). Washing with 1% aqueous ethanol (1 l.) eluted the monosaccharide fraction, which was concentrated to a syrup *in vacuo*, extracted with methanol, and de-ionised by treatment of the aqueous solution with small amounts of Amberlite IR-4B(OH^-) and Amberlite IR-120 (H^+). The freeze-dried product (68 mg., 87%) had $[\alpha]_D^{17}$ −84·9° (*c* 1 in H_2O) and behaved, on paper chromatography and paper ionophoresis, in the same way as fructose. Only traces of glucose were present.

The disaccharide fraction was eluted with 5% (v/v) aqueous ethanol (1 l.) and was purified as above. The freeze-dried product (121·2 mg., 82%) had $[\alpha]_D$ +119·2° (*c* 1·7 in H_2O) (Montgomery *et al.*[10] give +120° for *iso*maltose). In the region 1027—715 cm.$^{-1}$ its infrared spectrum was identical with that of *iso*maltose. Treatment of a portion (30 mg.) with acetic anhydride (1·5 c.c.) and sodium acetate (15 mg.) at 100—110° for 3 hr. gave crystalline β-*iso*maltose octa-acetate (5 mg.), m. p. and mixed m. p. 144—145°.

(v) *Periodate oxidation of trisaccharide X.* Trisaccharide X (40 mg.) and anhydrous raffinose (37·4 mg.) were severally dissolved in water (1 c.c.) and treated with 0·5M-sodium metaperiodate (1 c.c.) at 18°; changes in $[\alpha]_D^{18}$ were :

Time (min.)	0	3	7	20	60	120	300	600
Raffinose	+124·1°	+86	+78	+73	+64	+56	+50	+48·2
Trisaccharide X	+102·5°	+88	+76	+69	+62	+55	+47	+46·0

After 600 min., part (1·7 c.c.) of each solution was diluted to 5 c.c. Portions (2·5 c.c.) of these solutions were then used for determination of periodate consumption and formic acid (see above).

(vi) *Methylation of trisaccharide X.* The trisaccharide (25 mg.) was methylated in dioxan (2 c.c.) with ten portions each of 30% sodium hydroxide and dimethyl sulphate (total vol. 3·6 and 1·8 c.c. respectively) as described for kestose.[11] The product (10·5 mg.) was hydrolysed with 2N-sulphuric acid at 100° for 2 hr., then neutralised, and the filtrate freeze-dried. Paper chromatography, with naphtharesorcinol for selective identification of ketoses, showed components, *inter alia*, having R_F values of 2 : 3 : 4-tri- and 2 : 3 : 4 : 6-tetra-*O*-methylglucose and a tetra-*O*-methylfructose.

Characterisation of Panose.—The two crops of crystals isolated during separation of the oligosaccharide mixture were recrystallised from aqueous methanol and had m. p. 218—220°, undepressed on admixture with panose, and showed $[\alpha]_D^{18}$ +153·1° (equil.; *c* 1 in H_2O). On

[8] Trevelyan, Proctor, and Harrison, *Nature*, 1950, **166**, 444.
[9] Foster, *J.*, 1953, 982.
[10] Montgomery, Weakley, and Hilbert, *J. Amer. Chem. Soc.*, 1949, **71**, 1682.
[11] Albon, Bell, Blanchard, Gross, and Rundell, *J.*, 1953, 24.

paper chromatography or paper ionophoresis its behaviour was identical with that of panose, and analysis of its partial hydrolysate showed the presence of *iso*maltose, maltose, glucose, and unchanged panose.

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396. *The Separation of Reducing Carbohydrates as their N-Substituted Glycosylammonium Ions.*

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A rapid method for the paper-ionophoretic separation of a homologous series of reducing oligosaccharides as their *N*-benzylglycosylammonium ions is described. The rates of migration of such ions can be used to determine the molecular sizes of oligosaccharides.

ONE of the problems encountered in the paper-chromatographic separation of oligosaccharides was their low R_F values in many solvents. In attempts to overcome this, the rate of flow of solvent has been increased by running the chromatograms [1] at 37° and a wide range of solvents has been investigated.[2] Separation of oligosaccharides as their benzylamine derivatives [3] is more rapid, taking only 18 hr. for derivatives containing up to five glucose units, but is still lengthy in comparison with the separation of certain oligosaccharides as their borate complexes by paper ionophoresis.[4] Although the latter affords some evidence as to the linkage of the reducing sugar it is not usually possible to determine the molecular size of an unknown sugar. Thus the homologous series of glucosaccharides containing 1 : 3- or 1 : 6-links can be separated but the series containing 1 : 4- (and presumably 1 : 2)-links show negligible separation.

We now report fully [5] a method whereby any reducing oligosaccharide, pentose, hexose, or heptose can be speedily separated by paper ionophoresis of its *N*-benzylglycosylammonium ion. These ions move at rates inversely related to their molecular weights and, to the first approximation, independent of the stereochemistry and mode of linkage of the sugar. Attempts are also described to use other amines of lower molecular weight in order to increase the relative separation of a homologous series.

EXPERIMENTAL

Standard Method of Separation of N-Benzylglycosylammonium Ions.—Each reducing sugar and reference sugar (5 μl. of 3% solution) was spotted along a line drawn on a strip (22·5 × 5 in.) of Whatman No. 3 paper and a benzylamine–methanol–10N-formic acid mixture (1 : 9 : 5; 5 μl.) superimposed. After the papers had been kept at 95° for 5 min. the *N*-benzylglycosylammonium ions were separated by ionophoresis at 600 v for 6 hr. (or 500 v for 15 hr. for higher saccharides) in an electrolyte (pH 1·8) composed of 5% aqueous sodium hydroxide (600 c.c.) and 90% formic acid (400 c.c.). After drying, the sugars and their complexes were detected with alkaline silver nitrate [6] or periodate followed by benzidine.[7] The mobility (M) of any component was expressed as the ratio of the distances separating (*a*) the *N*-benzylglycosylammonium ion from the unchanged sugar and (*b*) the *N*-benzylglycosylammonium ion from unchanged glucose.

[1] Hough, Jones, and Wadman, *J.*, 1950, 1702.
[2] Jeanes, Wise, and Dimler, *Analyt. Chem.*, 1951, **23**, 415.
[3] Bayly and Bourne, *Nature*, 1953, **171**, 385.
[4] Foster, *J.*, 1953, 982.
[5] Cf. Barker, Bourne, Grant, and Stacey, *Nature*, 1956, **177**, 1125.
[6] Trevelyan, Proctor, and Harrison, *ibid.*, 1950, **166**, 444.
[7] Cifonelli and Smith, *Analyt. Chem.*, 1954, **26**, 1132.

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TABLE 1. *Mobilities of* N*-benzylglycosylammonium ions.*

Sugar	Mobility (M)	Ratio (X) *	Sugar	Mobility (M)	Ratio (X) *
D-Arabinose	1·14	1·13	Laminaribiose	0·79	0·63
L-Arabinose	1·15	1·13	Maltose	0·75	0·63
D-Ribose	1·11	1·13	Melibiose	0·77	0·63
D-Xylose	1·09	1·13	Nigerose	0·78	0·63
L-Xylose	1·12	1·13			
			Cellotriose	0·57	0·46
D-Galactose	1·00	1·00	Isomaltotriose	0·62	0·46
D-Glucose	1·00	1·00	Laminaritriose	0·63	0·46
3-deoxy-	1·04	1·06	Maltotriose	0·61	0·46
3-*O*-methyl-	0·95	0·95	Nigerian trisaccharide	0·60	0·46
2 : 3-di-*O*-methyl-	0·92	0·91	Panose	0·59	0·46
2 : 3 : 6-tri-*O*-methyl-	0·90	0·87			
2 : 3 : 4 : 6-tetra-*O*-methyl-	0·88	0·83	Laminaritetraose	0·51	0·36
D-Mannose	1·00	1·00	Maltotetraose	0·49	0·36
L-Rhamnose	1·02	1·06			
			Maltopentaose	0·42	0·29
D-*glycero*-D-*gala*Heptose	0·91	0·90			
			Maltohexaose	0·33	0·25
Cellobiose	0·71	0·63			
3-(1-β-Glucosyl)xylose	0·80	0·67	D-Fructose	1·00	1·00
Isomaltose	0·78	0·63	L-Sorbose	1·00	1·00
Lactose	0·72	0·63	D-*gluco*Heptulose	0·90	0·90

* X = (Mol. wt. of N-benzylglucosylammonium ion)/(mol. wt. of N-benzylglycosylammonium ion.

TABLE 2. *Mobilities of* N*-methylglycosylammonium ions.*

Sugar	Mobility ($M1$)	Ratio ($X1$) *	Sugar	Mobility ($M1$)	Ratio ($X1$) *
D-Ribose	1·17	1·18	Laminaribiose	0·65	0·54
			Maltose	0·62	0·54
D-Galactose	1·00	1·00	Melibiose	0·63	0·54
D-Glucose	1·00	1·00			
D-Mannose	1·00	1·00	Maltotriose	0·45	0·38
			Maltotetraose	0·34	0·29
D-*glycero*-D-*gala*Heptose	0·89	0·87	Maltopentaose	0·23	0·23
Cellobiose	0·61	0·54	Maltohexaose	0·20	0·19
Lactose	0·61	0·54	D-Fructose	1·00	1·00

* $X1$ = (Mol. wt. of N-methylglucosylammonium ion)/(mol. wt. of N-methylglycosylammonium ion).

TABLE 3. *Mobilities of glycosylammonium ions.*

Sugar	Mobility ($M2$)	Ratio ($X2$) *	Sugar	Mobility ($M2$)	Ratio ($X2$) *
D-Arabinose	1·25	1·20	Lactose	0·59	0·53
L-Arabinose	1·26	1·20	Laminaribiose	0·64	0·53
D-Ribose	1·22	1·20	Maltose	0·60	0·53
D-Xylose	1·21	1·20	Melibiose	0·62	0·53
L-Xylose	1·24	1·20	Nigerose	0·63	0·53
D-Galactose	1·00	1·00	Cellotriose	0·41	0·36
D-Glucose	1·00	1·00	Isomaltotriose	0·45	0·36
3-deoxy-	1·12	1·10	Laminaritriose	0·44	0·36
3-*O*-methyl-	0·95	0·93	Maltotriose	0·45	0·36
2 : 3-di-*O*-methyl-	0·89	0·87	Panose	0·43	0·36
2 : 3 : 6-tri-*O*-methyl-	0·85	0·81			
2 : 3 : 4 : 6-tetra-*O*-methyl-	0·81	0·76	Laminaritetraose	0·34	0·27
D-Mannose	1·00	1·00	Maltotetraose	0·31	0·27
			Maltopentaose	0·24	0·22
D-*glycero*-D-*gala*Heptose	0·88	0·86	Maltohexaose	0·19	0·18
Cellobiose	0·58	0·53	D-Fructose	1·00	1·00
Isomaltose	0·63	0·53	D-*gluco*Heptulose	0·88	0·86

* $X2$ = (Mol. wt. of glucosylammonium ion)/(mol. wt. of glycosylammonium ion).

Standard Method of Separating N-*Methylglycosylammonium Ions.*—The *N*-methylglycosylammonium ions were produced on Whatman No. 3 paper by superimposing on the sugar (5 μl. of 3% solution) one spot (5 μl.) of a solution obtained by passing methylamine (equivalent to 1 c.c.) into a mixture of methanol (9 c.c.) and 10N-formic acid (5 c.c.). The paper was heated for 5 min. at 90° and the *N*-methylglycosylammonium ions were separated by ionophoresis and detected as described for the *N*-benzyl derivatives. The mobility (*M*1) was expressed as the ratio of the distances separating the *N*-methylglycosylammonium ion from the unchanged sugar and the *N*-methylglucosylammonium ion from unchanged glucose.

Standard Method of Separation of Glycosylammonium Ions.—These ions were formed on Whatman No. 3 paper by superimposing on the sugar (5 μl. of 3% solution), one spot (5 μl.) of a solution of ammonium formate (1 g.) in methanol (10 c.c.). The papers containing hexoses and oligosaccharides were heated for 5 min. at 85° and those containing pentoses for 3 min. at 85°. The glycosylammonium ions were separated by ionophoresis and detected as described above for the *N*-benzyl derivatives. The mobility (*M*2) was expressed as the ratio of the distances separating the glycosylammonium ion from the unchanged sugar and the glucosylammonium ion from unchanged glucose.

Discussion

Initial experiments showed that the *N*-benzylglycosylamines produced by the paper-chromatographic method of Bayly and Bourne [3] could be detected by alkaline silver nitrate,[6] periodate,[7] and aniline hydrogen phthalate [8] in addition to ninhydrin. The suitability of these sprays for detection of the *N*-benzylglycosylammonium ions under the various conditions used in ionophoresis is commented upon in the appropriate sections.

Choice of Electrolyte.—The known stability [9] of glycosylammonium ions at pH 2 led to the employment of an acidic electrolyte and initial experiments were carried out with hydrochloric acid at pH 2. The proportion of *N*-benzylmaltosylammonium ion to unchanged maltose was low under these conditions but was increased by the addition of sodium chloride to the electrolyte. The amount that could be added was limited because the increased conductivity gave rise to extra heat, which it was difficult to dissipate. Also, the high chloride content of the paper reduced the sensitivity of the alkaline silver nitrate method of detection. Streaking of spots was encountered when acetic acid (8N and 2N), acetate (pH 3·1), or formic acid (pH 2) was used, but a mixture of 5% aqueous sodium hydroxide (600 c.c.) and 90% formic acid (400 c.c.) gave satisfactory results. The pH of the electrolyte stayed constant at 1·8 during ionophoresis. The formic acid was removed by heating the paper, and the residual sodium formate did not appreciably reduce the sensitivity of the silver nitrate method of detection.

Formation of the Sugar–Benzylamine Complex.—With maltose as a guide, the optimum conditions for the formation of the benzylamine complex were found to be 95° for 5 min. It was desirable to commence ionophoresis directly the *N*-benzylglycosylamine had been formed. It was appreciated that the presence of excess of benzylamine initially would increase the pH near the spot. This was overcome by adding 10N-formic acid (5 c.c.) to the benzylamine (1 c.c.) in methanol (9 c.c.) which was superimposed on the sugar. The optimum heating conditions remained the same but there was considerably higher conversion (*ca.* 70%) of the sugar into the *N*-benzylglycosylammonium ion. It may be that the formic acid catalysed it.[10]

Detection of the N-*Benzylglycosylammonium Ion.*—A method of detection based on the sugar part of the molecule was desirable because the sensitivity would then be largely independent of the molecular size of the oligosaccharide. Although the silver nitrate method [6] was sensitive enough in most cases, it failed to detect benzylamine complexes of 2-methyl derivatives of glucose. These were, however, located by using a fluorescent

[8] Partridge, *Nature*, 1949, **164**, 443.
[9] Isbell and Frush, *J. Amer. Chem. Soc.*, 1950, **72**, 1043.
[10] Cameron, *ibid.*, 1927, **49**, 1759; Bayly, Bourne, and Stacey, *Nature*, 1952, **169**, 876.

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screen to detect the ultraviolet light absorption.[11] Aniline hydrogen phthalate [8] showed only a slight reaction with *N*-benzylglycosylammonium ions. Detection by periodate followed by benzidine [7] was found to be suitable providing the amount of the ion present was known approximately.

Choice of Support.—Whatman No. 1 paper can be substituted for Whatman No. 3 with the advantage that a lower current results for a given voltage. An attempt was made to use fibreglass paper. Unfortunately there is a large endosmotic flow towards the cathode which markedly decreases the absolute distance of migration of a cation which can be achieved on a given length of paper. Also the fibreglass holds more electrolyte than paper and thus becomes more difficult to cool.

Use of Other Amines.—It was realised that use of an amine having a lower molecular weight or one that would give rise to a doubly charged ion might increase the relative separation or speed of separation of a homologous series of oligosaccharides. Methylamine formate and ammonium formate both led to the formation of their corresponding ions which showed the expected increased mobilities. Optimum conditions were determined but these ions, particularly the glycosylammonium ions, were more unstable and occasionally more than one positive ion was obtained from a given sugar.[10] Spots of D-xylose and ammonium formate (10%) in methanol were heated for various times at 85° and then submitted to ionophoresis. The amount of D-xylosylammonium ion formed increased to a maximum after 3 minutes' heating; none could be detected after heating for longer than 5 minutes. Other ions were produced after various times with mobilities 0·816 (after 2·5 min.), 0·64 (after 3 min.), and 0·15 (after 5 min.). Glucosylammonium ions, although more stable, underwent a similar decomposition giving ions with mobilities 1·00, 0·63, 0·49, and 0·12. One of the decomposition products was presumably formed by condensation to give a diglycosylammonium ion. The mobility (*M*3) of a diglycosylammonium ion was expressed as the ratio of the distances separating the diglycosylammonium ion from the unchanged sugar and the glucosylammonium ion from unchanged glucose (see Table 4). Evidence for the molecular weight of these ions was provided by the following comparisons of mobilities: diglucosylammonium 0·63, maltosylammonium 0·60; dimaltosylammonium 0·33, maltotetraosylammonium 0·31; dimaltotriosylammonium 0·24, maltohexaosylammonium 0·19.

TABLE 4. *Mobilities of diglycosylammonium ions.*

Ion	Mobility (*M*3)	Ratio (*X*3) *	Ion	Mobility (*M*3)	Ratio (*X*3) *
Diarabinosylammonium	0·82	0·64	Dimaltotriosylammonium	0·24	0·18
Diglucosylammonium	0·63	0·53	Dimaltotetraosylammonium ...	0·15	0·14
Di-D-*glycero*-D-*gala*heptosylammonium	0·53	0·45	Dimaltopentaosylammonium	0·12	0·11
Dimaltosylammonium	0·33	0·27	Dimaltohexaosylammonium ...	0·09	0·09

* *X*3 = (Mol. wt. of glucosylammonium ion)/(mol. wt. of diglycosylammonium ion)

Glucose has been condensed with dimethylamine in methanol and formic acid by heating them at 90° for 5 min. Ionophoresis with formate (pH 1·8), followed by development of the paper with alkaline silver nitrate, showed that the *N*-dimethylglucosylammonium ion was formed in good yield. Condensation of glucose with aniline in methanol and formic acid at 85° for 5 min. gave only a small amount of *N*-phenylglucosylammonium ion. 2-Aminopyridine also gave a poor conversion and the spot detected corresponded to an ion carrying only one positive charge. No positive ion was observed when using glucose and 2 : 4-dinitrophenylhydrazine, hydrazine, or hydroxylamine.

Table 5 illustrates the inverse relation between the mobility and molecular weight of some of these substituted glucosylammonium ions. The mobility (*M*4) of such an ion was the ratio of distances separating it and the *N*-benzylglucosylammonium ion from unchanged glucose.

[11] Jones and Marsh, unpublished work.

TABLE 5. *Comparative mobilities of substituted glucosylammonium ions.*

Ion	Mobility (*M*4)	Ratio (*X*4) *	Ion	Mobility (*M*4)	Ratio (*X*4) *
N-Benzylglucosylammonium ...	1·00	1·00	*N*-Dimethylglucosylammonium	1·27	1·30
N-Phenylglucosylammonium ...	1·02	1·05	*N*-Methylglucosylammonium ...	1·28	1·39
N-Pyridylglucosylammonium	1·02	1·05	Glucosylammonium	1·32	1·50

* *X*4 = (Mol. wt. of *N*-benzylglucosylammonium ion)/(mol. wt. of the ion).

Other Observations.—Non-reducing sugars, *e.g.*, sucrose, αα-trehalose, raffinose, and methyl α-D-glucoside did not react with benzylamine. When fructose was heated with benzylamine formate the spot became brown and conversion into the positive ion was only about 20%. In the paper-chromatographic method *N*-benzylfructosylamine was unstable. The *N*-benzyl-2-deoxyglucosylammonium ion was unstable but the *N*-benzyl-3-deoxyglucosylammonium ion was formed in a poor yield.

In all the above experiments the relative mobilities of the ions were reproducible ($M \pm 0{\cdot}015$) but the absolute mobilities varied owing to many factors.[12] Ions placed near the edge of the paper tended to move more slowly and in each experiment suitably placed markers were used.

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THE UNIVERSITY, BIRMINGHAM, 15. [*Received, January 9th*, 1957.]

[12] Bourne, Foster, and Grant, *J.*, 1956, 4311.

397. *A New Preparation of Steroid Halides.*

By J. BROOME, B. R. BROWN, and G. H. R. SUMMERS.

Aluminium and titanium halides have been shown to react with 3β-hydroxy-Δ⁵-steroids, and their acetates, to give the corresponding halides in good yields. Reaction of androst-5-ene-3β : 17β-diol with aluminium chloride caused selective replacement of the 3β-hydroxyl group. A new preparation of aluminium iodide is described.

IT has been known for some years [1] that simple aliphatic alcohols can be converted into the corresponding chlorides in good yields by treatment with aluminium chloride at 140—150°. Possibly owing to its vigorous nature this reaction has not been applied to more complex alcohols, nor have other aluminium halides been used. We now report its extension in a modified form to the halogenation of 3β-hydroxy-Δ⁵-steroids, *viz.*, in refluxing ether in the presence of 10—15 mols. of aluminium halide for 8 hr. : the yields of halide were between 70 and 100%. Direct replacement by chlorine of the 3α-hydroxyl group in *epi*cholesterol failed, giving cholesta-3 : 5-diene as the sole product (cf. Evans and Shoppee [2]).

A new preparation of aluminium iodide has been developed which is more convenient for organic chemical purposes than that previously described.[3] This involves reaction of amalgamated aluminium with iodine under ether. The formation of cholesteryl iodide by use of this reagent constitutes a direct preparation superior to that reported by Landauer and Rydon [4] using triphenyl phosphite methiodide as the iodinating agent. It is noteworthy that the reaction is equally successful with the acetates of the above sterols.

Cholestan-3β-ol under similar conditions is recovered unchanged. Consequently the aluminium halide reagent has been used to replace selectively an activated hydroxyl group in a polyhydroxy-steroid. Thus androst-5-ene-3β : 17β-diol gave 3β-chloroandrost-5-en-17β-ol in a 56% yield. This reaction was slower than the corresponding reactions with

[1] Norris and Sturgis, *J. Amer. Chem. Soc.*, 1939, **61**, 1413.
[2] Evans and Shoppee, *J.*, 1953, 546.
[3] Eley and King, *Trans. Faraday Soc.*, 1951, **47**, 1288.
[4] Landauer and Rydon, *J.*, 1953, 2224.

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monohydroxy-compounds and even after 24 hours some of the original diol was recovered. It seems evident that some interaction between a double bond near the hydroxyl group and the aluminium halide is essential for replacement to occur and retention of configuration results. This is reminiscent of the situation, already commented on,[5] in the reaction between ketones and the reagent aluminium chloride–lithium aluminium hydride. Some qualitative evidence for such interaction has been obtained from the observations that the ultraviolet spectrum, fluorescent properties, and optical rotation of cholesterol in ether change on the addition of aluminium chloride, whereas those of cholestan-3β-ol are unaffected. These effects are being investigated quantitatively.

Titanium tetrachloride and tetrabromide also convert cholesterol into the corresponding halides quantitatively.

Experimental

Cholesteryl Chloride.—(*a*) Cholesterol (568 mg.) in dry ether (40 ml.) was boiled under reflux for 8 hr. with anhydrous aluminium chloride (3·5 g.). The cold ethereal solution was shaken with 10% aqueous sodium hydroxide, washed with water, and dried. Evaporation of the ether gave a pale yellow oil (525 mg.) which quickly crystallised. Recrystallisation from acetone yielded cholesteryl chloride as colourless needles, m. p. and mixed m. p. 97°, $[\alpha]_D^{20}$ −26° (in $CHCl_3$) (Found : C, 79·8; H, 11·25. Calc. for $C_{27}H_{45}Cl$: C, 80·1; H, 11·1%).

(*b*) Cholesterol (1·00 g.) in dry ether (100 ml.) was treated with titanium tetrachloride (2·8 ml.). After an initial vigorous reaction the orange solution was boiled for 4 hr. The resulting brown solution, on being treated as above, gave a colourless oil which was dissolved in pentane, filtered through alumina, and crystallised from acetone to give cholesteryl chloride (940 mg.), m. p. 96—97° (Found : C, 79·6; H, 11·2%).

(*c*) A similar experiment, as in (*a*) but with cholesteryl acetate (382 mg.), yielded (after chromatography on alumina) cholesteryl chloride (345 mg.), m. p. and mixed m. p. 97—98° (Found : C, 79·8; H, 10·8%).

Cholesteryl Bromide.—(*a*) After reaction as in the preparation of the chloride but with cholesterol (560 mg.), aluminium bromide (3·5 g.), and ether (40 ml.), evaporation yielded a red oil which was dissolved in pentane and filtered through a column of alumina (20 g.). Evaporation gave a solid (635 mg.) which by recrystallisation from acetone gave cholesteryl bromide as colourless elongated plates, m. p. and mixed m. p. 102—103°, $[\alpha]_D^{17}$ −18° (in $CHCl_3$) (Found : C, 72·05; H, 10·2. Calc. for $C_{27}H_{45}Br$: C, 72·2; H, 10·0%).

(*b*) Cholesterol (200 mg.) in ether (20 ml.) was boiled with titanium tetrabromide (700 mg.) for 3·5 hr. Isolation of the product in the usual way gave an oil which after filtration of a pentane solution through alumina gave an oil (198 mg.) which by crystallisation from acetone gave cholesteryl bromide, m. p. 98—99° (Found : C, 71·95; H, 10·1%).

Cholesteryl Iodide.—Aluminium powder (3·0 g.) was shaken with a 1% solution of mercuric chloride in commercial ether (25 ml.) for about 2 min. The resulting grey powder was washed by decantation with dry ether and treated gradually with iodine (38 g.) in ether (350 ml.) so that the reaction did not become too vigorous. The reaction was completed under reflux for 30 min., all the aluminium dissolving. (In a quantitative experiment in which the excess of iodine was determined by titration, 0·269 g. of aluminium reacted with 3·74 g. of iodine.) (Found : I, 93·3. Calc. for AlI_3 : I, 93·4%).

Cholesterol (5·5 g.) in ether (50 ml.) was added to the aluminium iodide solution and the mixture was boiled for 8 hr., then decomposed at 0° with aqueous sodium hydroxide. The ether layer was separated and washed successively with water, aqueous sodium hydrogen sulphite, and water, and dried. Evaporation yielded a dark brown oil (5·1 g.) which was dissolved in pentane and filtered through a column of alumina (140 g.). Evaporation of the eluate (500 ml.) and crystallisation of the residue from acetone yielded cholesteryl iodide (4·7 g.) as colourless needles, m. p. and mixed m. p. 107—108°, $[\alpha]_D^{17}$ −12° (in $CHCl_3$) (Found : C, 65·7; H, 9·1. Calc. for $C_{27}H_{45}I$: C, 65·3; H, 9·05%).

Stigmasteryl Chloride.—Stigmasterol (50 mg.) in ether (5 ml.) was boiled with anhydrous aluminium chloride (300 mg.) for 4 hr. Working up in the usual way gave stigmasteryl chloride (48 mg.) which by crystallisation from acetone gave plates, m. p. 88—89° (Found : C, 80·9; H, 10·7; Cl, 8·3. Calc. for $C_{29}H_{47}Cl$: C, 80·8; H, 11·0; Cl, 8·2%).

[5] Broome and Brown, *Chem. and Ind.*, 1956, 1307.

β-Sitosteryl Chloride.—β-Sitosterol (100 mg.) in ether (25 ml.) was boiled with anhydrous aluminium chloride (700 mg.) for 8 hr. Isolation of the product in the usual way gave an oil (94 mg.) which by crystallisation from acetone gave β-sitosteryl chloride as prisms, m. p. 87—88° (Found: C, 80·5; H, 11·4; Cl, 8·0. Calc. for $C_{29}H_{49}Cl$: C, 80·4; H, 11·4; Cl, 8·2%).

β-Sitosteryl Bromide.—This was prepared as above from sitosterol (100 mg.) and aluminium bromide (800 mg.). The oil (101 mg.) by crystallisation from acetone gave β-sitosteryl bromide as plates, m. p. 77—78° (Found: C, 73·0; H, 10·6; Br, 16·5. Calc. for $C_{29}H_{49}Br$: C, 72·9; H, 10·35; Br, 16·7%).

3β-Chloroandrost-5-en-17β-ol.—Androst-5-ene-3β : 17β-diol (180 mg.) in ether (100 ml.) was boiled with aluminium chloride (3·0 g.) for 24 hr. The mixture was worked up as usual, to yield an oil. This was dissolved in benzene and put on a column of alumina. Elution with 4 : 1 benzene–ether (200 ml.) yielded colourless crystals (80 mg.). 3β-Chloroandrost-5-en-17β-ol, purified by recrystallisation from methanol or by sublimation at 150°/17 mm., was obtained as colourless needles, m. p. 163—164°, $[\alpha]_D^{16}$ −45° (in $CHCl_3$) (Found: C, 74·1; H, 9·5; Cl, 11·1. Calc. for $C_{19}H_{29}OCl$: C, 73·9; H, 9·4; Cl, 11·5%). Kuwada and Miyasaka [6] give m. p. 163°.

Further elution with ether (300 ml.) gave unchanged starting material (45 mg.), m. p. and mixed m. p. 177—178°.

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[6] Kuwada and Miyasaka, *J. Pharm. Soc. Japan*, 1937, **57**, 234.

398. *The Preparation of β-Amino-alcohols.*

By J. H. Hunt and D. McHale.

Reduction of α-benzamido-acids with lithium aluminium hydride gives β-benzylamino-alcohols which may be readily debenzylated to β-amino-alcohols. The method is particularly convenient for the preparation of optically active β-amino-alcohols. Resolution of DL-α-amino-α-*cyclo*hexyl-acetic acid is described.

The reduction of amino-acids with lithium aluminium hydride in ether is often unsatisfactory, not only because of inherent low solubility of the acids in ether, but also owing to the formation of insoluble inorganic complexes which prevent complete reaction. To overcome this difficulty, Dornow, Messwarb, and Frey [1] used a mixture of ether and tetrahydrofuran in the reduction of tyrosine by lithium aluminium hydride, and Vogl and Pöhm [2,3] reduced several amino-acids in tetrahydrofuran alone. Karrer and his co-workers reported reductions of several amino-esters [4] and also of the benzoyl derivatives of histidine ethyl ester, in which reduction was accompanied by debenzoylation.[5] The reduction of *N*-acetyl-, *N*-formyl-, and *N*-ethoxycarbonyl-amino-acids or their ethyl esters has also been reported.[1,3,6]

We have found that many benzamido-acids are sufficiently soluble in ether to be reduced with lithium aluminium hydride, giving in most cases good yields of the corresponding benzylamino-alcohols.

With optically active amino-acids this method is particularly convenient as the *N*-benzoyl derivatives are those most frequently used for their resolution and the resolved compounds can be reduced directly without isolating the free acids. Moreover, the benzylamino-alcohols can be debenzylated by catalytic hydrogenolysis,[7] which minimises racemisation of the amino-alcohols.

[1] Dornow, Messwarb, and Frey, *Chem. Ber.*, 1950, **83**, 445.
[2] Vogl and Pöhm, *Monatsh.*, 1952, **83**, 541.
[3] *Idem, ibid.*, 1953, **84**, 1097.
[4] (*a*) Karrer, Portmann, and Suter, *Helv. Chim. Acta*, 1948, **31**, 1619; (*b*) Karrer and Portmann, *ibid.*, p. 2088.
[5] Karrer, Suter, and Waser, *ibid.*, 1949, **32**, 1936; Karrer and Saemann, *ibid.*, 1953, **36**, 570.
[6] Wessely and Swoboda, *Monatsh.*, 1951, **82**, 621; Berlinguet, *Canad. J. Chem.*, 1954, **32**, 31.
[7] Stoll, Peyer, and Hofmann, *Helv. Chim. Acta*, 1943, **26**, 929.

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Benzylamino-alcohols have thus been obtained from hippuric acid, benzoyl-D- and -L-alanine, benzoyl-DL-valine, benzoyl-L-phenylalanine, and benzoyl-L-glutamic acid. In most cases it was convenient to use the Soxhlet extraction procedure of Nystrom and Brown;[8] otherwise solutions or suspensions of the benzamido-acids were used.

In most of the experiments, 3 mols. (100% excess) of lithium aluminium hydride were used and reaction times were 5—20 hr., though hippuric acid was not completely extracted after 70 hr. Under these conditions, both carboxyl and amide groups were usually reduced, although small amounts of benzamido-alcohols were sometimes isolated: in one experiment with benzoyl-L-glutamic acid in tetrahydrofuran (reaction time 75 min.) the main product was L-2-benzamidopentane-1 : 5-diol. Slow reduction of monosubstituted amides by lithium aluminium hydride has been noted before.[9]

The reaction mixtures were worked up by addition of the theoretical amount of water, giving a solid which was easily filtered off and from which the benzylamino-alcohol (in most cases freely ether-soluble) was readily extracted. This is in marked contrast to those procedures which give as the main product unsubstituted amino-alcohols which are frequently of low solubility in ether and difficult to remove from the mass of inorganic material.

By this method D- and L-α-benzamido-α-phenylacetic acid gave D- and L-2-benzylamino-2-phenylethanol; the L-isomer was also obtained by resolving the DL-form with di-*p*-toluoyl-L-tartaric acid. D-2-Benzylamino-2-phenylethanol gave crystalline D-2-amino-2-phenylethanol ($[\alpha]_D^{25}$ −27·2°) of higher optical purity than that prepared as a liquid by Ovakimian, Kuna, and Levene[10] ($[\alpha]_D^{25}$ −15°).

Since completion of our work, Arpesella and La Manna[11] reported the preparation of both isomers by lithium aluminium hydride reduction of the ethyl α-amino-α-phenylacetates. Their values for the D-isomer agree with ours.

(+)-α-Amino-α-*cyclo*hexylacetic acid prepared by hydrogenation of (+)-α-amino-α-phenylacetic acid was described by Reihlen and Knöpfle[12] who indirectly related the configuration of the latter acid to L-(+)-valine. We have prepared DL-α-amino-α-*cyclo*hexylacetic acid by hydrogenating α-amino-α-phenylacetic acid and have resolved the benzoyl derivative with quinine, obtaining D- and L-α-benzamido-α-*cyclo*hexylacetic acid. Hydrolysis of the benzoyl-D-acid gave D-α-amino-α-*cyclo*hexylacetic acid, $[\alpha]_D^{25}$ −33·8° in 5N-HCl. Reihlen and Knöpfle found $[\alpha]_D$ −31° in 0·5N-HCl, and Rudman, Meister, and Greenstein,[13] using an enzymic method of resolution claimed to give a product of >99·9% purity, obtained $[\alpha]_D^{26}$ −35·0° in 5N-HCl. The benzoyl-L-acid has been reduced to L-2-benzylamino-2-*cyclo*hexylethanol and debenzylated to L-2-amino-2-*cyclo*hexylethanol.

Experimental

2-Benzylaminoethanol.—Hippuric acid (12 g.), in a Soxhlet extractor, was reduced with lithium aluminium hydride (8·4 g., 3·3 mols.) in dry ether (300 ml.) under nitrogen, by Nystrom and Brown's procedure.[8] After 70 hr. some hippuric acid (2·8 g.) remained undissolved and was rejected. Water (10 ml.) was added dropwise to the cooled mixture, and the insoluble material filtered off and washed with ether. The oil (6·3 g.) remaining after evaporation of the combined ether solutions was distilled, giving the amino-alcohol (4 g.), b. p. 106—107°/0·5 mm., $n_D^{20\cdot5}$ 1·5419 (Found: C, 71·4; H, 8·5; N, 9·05. Calc. for $C_9H_{13}ON$: C, 71·5; H, 8·7; N, 9·3%). The picrate had m. p. 134° (lit.,[14] 134—135°) (Found: C, 47·7; H, 4·3; N, 14·4. Calc. for $C_{15}H_{16}O_8N_4$: C, 47·4; H, 4·2; N, 14·7%).

D-*2-Benzylaminopropanol.*—By the same procedure benzoyl-D-alanine (7·7 g.) was reduced during 3 hr. with lithium aluminium hydride (4·5 g., 3 mols.) in ether (300 ml.). The product (4·6 g.), obtained as before, recrystallised from hot *cyclo*hexane (10 ml.) on addition of light

[8] Nystrom and Brown, *J. Amer. Chem. Soc.*, 1947, **69**, 2548.
[9] *E.g.*, Mićović and Mihailović, *J. Org. Chem.*, 1953, **18**, 1190.
[10] Ovakimian, Kuna, and Levene, *J. Biol. Chem.*, 1940, **135**, 91.
[11] Arpesella and La Manna, *Il Farmaco*, 1953, **8**, 212.
[12] Reihlen and Knöpfle, *Annalen*, 1936, **523**, 199.
[13] Rudman, Meister, and Greenstein, *J. Amer. Chem. Soc.*, 1952, **74**, 551.
[14] Gabriel and Stelzer, *Ber.*, 1896, **29**, 2385.

petroleum (b. p. 40—60°; 25 ml.), giving needles (3·35 g.), m. p. 46·5°, $[\alpha]_D^{27.5}$ −44·5° (*c* 4 in EtOH) (lit.,[7] m. p. 47—49°, $[\alpha]_D^{23}$ −44·25°) (Found: C, 72·8; H, 8·8; N, 8·25. Calc. for $C_{10}H_{15}ON$: C, 72·7; H, 9·15; N, 8·5%). The hydrogen tartrate (from ethanol) had m. p. 94° undepressed with an authentic sample.[7]

L-2-*Benzylaminopropanol*.—By the same procedure benzoyl-L-alanine (19 g.) was reduced with lithium aluminium hydride (12·5 g., 3·3 mols.) in ether (500 ml.). The product (14·0 g.) had m. p. 45°, $[\alpha]_D^{21}$ +43·5° (*c* 4 in EtOH) (lit.,[7] m. p. 47—49°) (Found: C, 72·5; H, 9·1; N, 8·35. Calc. for $C_{10}H_{15}ON$: C, 72·7; H, 9·15; N, 8·5%). The hydrogen oxalate (prisms from ethanol) had m. p. 187° (lit.,[7] 187—189°) (Found: N, 5·3. Calc. for $C_{12}H_{17}O_5N$: N, 5·5%).

DL-2-*Benzylamino*-3-*methylbutanol*.—Benzoyl-DL-valine (7·8 g.), reduced as above with lithium aluminium hydride (4·0 g., 3 mols.) in dry ether (250 ml.), gave an oil (6·1 g.) which was distilled at 155—157°/9 mm., redistilled at 93—94°/0·01 mm. (5·36 g.), then having n_D^{14} 1·5212 (Found: C, 74·8; H, 9·8; N, 7·2. Calc. for $C_{12}H_{19}ON$: C, 74·6; H, 9·9; N, 7·25%). The picrate (from ethanol) melted at 128—129° (lit.,[7] 131—133°).

L-2-*Benzylamino*-3-*phenylpropanol*.—A solution of *N*-benzoyl-L-β-phenylalanine (1·6 g.) in dry ether (50 ml.) was added during 10 min. with stirring under nitrogen to lithium aluminium hydride (0·5 g., 2·2 mols.) in dry ether (25 ml.). After the initial vigorous reaction, the mixture was refluxed for 5 hr. and kept overnight. Water (1·2 ml.) was added, the precipitate filtered off, and the residue extracted with ether (Soxhlet) for 3 hr. The extract, together with the original ethereal filtrate, was evaporated and the residue digested with hot light petroleum (b. p. 60—80°; 100 ml.). The filtered solution, on cooling, deposited L-2-benzamido-3-phenylpropanol which, recrystallised from benzene, had m. p. 169° (lit.,[15] 169°) (Found: C, 75·1; H, 6·6; N, 5·1. Calc. for $C_{16}H_{17}O_2N$: C, 75·3; H, 6·7; N, 5·5%). The petroleum solution, on concentration, deposited L-2-*benzylamino*-3-*phenylpropanol* which recrystallised from light petroleum (b. p. 40—60°) in needles, m. p. 60—61°, $[\alpha]_D^{23}$ −8·3° (*c* 5·03 in EtOH) (Found: C, 79·6; H, 8·1; N, 5·6. $C_{16}H_{19}ON$ requires C, 79·65; H, 7·9; N, 5·8%). The *oxalate* had m. p. 208° (from alcohol) (Found: C, 65·1; H, 6·3; N, 3·7. $C_{18}H_{21}O_5N$ requires C, 65·2; H, 6·4; N, 4·2%).

L-2-*Amino*-3-*phenylpropanol*.—L-2-Benzylamino-3-phenylpropanol (0·48 g.) and hydrated oxalic acid (0·25 g.) were partially dissolved in 1 : 1 aqueous alcohol (30 ml.). 10% Palladium–charcoal (1 g.) was added, and the mixture was shaken with hydrogen for 2 hr. The catalyst was filtered off and washed, the filtrate and washings were evaporated under reduced pressure, and the residue was dried azeotropically with benzene and dissolved in alcohol (10 ml.). Ether (30 ml.) was added and the solid separating recrystallised from alcohol, giving L-α-(*hydroxymethyl*)*phenethylamine hydrogen oxalate*, m. p. 177° (0·16 g.) (Found: C, 54·8; H, 6·1; N, 5·2. $C_{11}H_{15}O_5N$ requires C, 54·8; H, 6·3; N, 5·8%), $[\alpha]_D^{23}$ *ca.* +1·9° (Karrer *et al.*[4a] give m. p. 161—163°). The oxalate (0·23 g.) was treated with 10% sodium hydroxide solution (4 ml.), and the base extracted with ether. The extract was dried (K_2CO_3), concentrated to about 10 ml., and filtered. After evaporation to 5 ml. and cooling (ice–salt), L-2-amino-3-phenylpropanol separated as plates, m. p. 90—91°, $[\alpha]_D^{23}$ −24·7° (*c* 3·1 in EtOH) (Oeda [15] gives m. p. 92—94°, $[\alpha]_D^{23}$ −24·4°; Karrer *et al.*[4a] give m. p. 85—86°, $[\alpha]_D^{17}$ −4·1°) (Found: C, 71·35; H, 8·8; N, 9·0. Calc. for $C_9H_{13}ON$: C, 71·5; H, 8·7; N, 9·3%).

Reduction of N-*Benzoyl*-L-*glutamic Acid*.—(*a*) Lithium aluminium hydride [2 g., 2·5 mols. (theor., 2·25 mols.)] was covered with tetrahydrofuran (40 ml.; purified by refluxing and distillation over sodium, redistillation over $LiAlH_4$), and to the stirred sludge under nitrogen was added during 15 min. a solution of benzoyl-L-glutamic acid (5 g.) (m. p. 134°, $[\alpha]_D$ −13·8°) in tetrahydrofuran (15 ml.). The mixture was then refluxed 1 hr., cooled in ice, and treated with water (5 ml.). The inorganic material was filtered off and washed with tetrahydrofuran (2 × 10 ml.). Evaporation of the filtrate and washings gave a syrup which crystallised and was triturated with ether. The crystals were filtered off (2 g.) and dissolved in methanol (charcoal), and the solution was filtered, diluted with ether (80 ml.), and cooled. L-2-*Benzamidopentane*-1 : 5-*diol* separated as needles and, recrystallised from benzene (50 ml.)–ethyl acetate (30 ml.), had m. p. 109°, $[\alpha]_D$ −28·6° (*c* 1·9 in EtOH) (Found: C, 64·9; H, 7·6; N, 6·4. $C_{12}H_{17}O_3N$ requires C, 64·3; H, 8·1; N, 6·2%).

(*b*) Benzoyl-L-glutamic acid (3·3 g.) in a Soxhlet extractor was reduced with lithium aluminium hydride (3·5 g., 7 mols.) in ether (150 ml.) under nitrogen during 20 hr. The mixture was cooled and treated with water (6 ml.), and the inorganic material filtered off and washed

[15] Oeda, *Bull. Chem. Soc. Japan*, 1938, **13**, 465.

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with ether. Evaporation of the ether gave a cloudy syrup which, on dissolution in benzene, slowly deposited crystals (0·2 g.) which after recrystallisation from ethyl acetate had m. p. 108° undepressed on admixture with the benzamido-diol above. The benzene mother-liquor was evaporated and the residual oil distilled. The fraction of b. p. 160°/0·01 mm. (0·6 g.) was dissolved in alcohol, and oxalic acid added (hydrated, 0·5 g.). Addition of ether (20 ml.) caused separation of L-2-*benzylaminopentane*-1 : 5-*diol mono*(*hydrogen oxalate*) which recrystallised from alcohol had m. p. 120°, $[\alpha]_D^{27}$ +8·1° (*c* 1·7 in H_2O) (Found : C, 55·95; H, 7·0; N, 4·3. $C_{14}H_{21}O_6N$ requires C, 56·2; H, 7·1; N, 4·7%).

α-*Amino*-α-cyclo*hexylacetic Acid*.—α-Amino-α-phenylacetic acid (7·5 g.) in 2N-hydrochloric acid (75 ml.) with Adams platinum catalyst (0·2 g.) was shaken with hydrogen. The theoretical volume (3 mols.) was taken up in 24 hr. The catalyst was filtered off, the filtrate made slightly alkaline with ammonia, and the separated acid filtered off, washed, and air-dried (6·8 g.; sublimes above 310°).

α-*Benzamido*-α-cyclo*hexylacetic Acid*.—The above acid (10·2 g.) was dissolved in water (50 ml.) by the addition of saturated sodium hydroxide solution (5·2 ml.). To the stirred mixture at 0°, benzoyl chloride (12·1 ml.) was added during 40 min., the solution being kept alkaline by the simultaneous addition of 4% sodium hydroxide solution. After a further hour's stirring the mixture was acidified with hydrochloric acid to Congo-red, and the precipitate filtered off and washed by stirring repeatedly with di*iso*propyl ether (3 × 15 ml.). Twice recrystallised from 1 : 1 aqueous alcohol (200 ml.) and dried (P_2O_5), the *acid* (14·2 g.) had m. p. 200° (Found : C, 68·9; H, 7·4; N, 5·4. $C_{15}H_{19}O_3N$ requires C, 68·95; H, 7·3; N, 5·4%).

The inactive acid (6·8 g.) and anhydrous quinine (8·45 g.) were dissolved in boiling 3 : 2-aqueous alcohol (130 ml.). The filtered solution was cooled to opalescence and seeded with a crystal of quinine salt from an initial experiment. Separation of quinine salt as small prisms commenced immediately and was completed by cooling and storage overnight. The filtered salt was washed with 3 : 2 aqueous alcohol (50 ml.) and recrystallised twice from the same solvent. After drying *in vacuo* at 100° (P_2O_5) *quinine* D-α-*benzamido*-α-cyclo*hexylacetate* (5 g.) had m. p. 149° after softening at 141°, $[\alpha]_D^{23}$ −112° (*c* 0·4 in EtOH) (Found : C, 69·5; H, 7·5; N, 6·85. $C_{35}H_{43}O_5N_3,H_2O$ requires C, 69·6; H, 7·5; N, 7·0%).

The quinine salt (8 g.), suspended in water (150 ml.), was acidified with dilute hydrochloric acid to Congo-red, and the mixture extracted with ether. The residue after evaporation of the dried ether solution, when recrystallised from benzene, gave the D-*benzamido-acid* (3 g.), m. p. 171—172°, $[\alpha]_D^{23}$ −26·1° (*c* 0·803 in 0·5N-NaOH) (Found : C, 69·2; H, 7·3; N, 5·05%).

D-α-*Amino*-α-cyclo*hexylacetic Acid*.—The D-benzamido-acid (1 g.) was refluxed with concentrated hydrochloric acid (40 ml.) and water (20 ml.) for 8 hr., then evaporated to dryness under reduced pressure and the residue freed from benzoic acid by several extractions with ether, redissolved in a little water, and made faintly alkaline with ammonia. The acid, which separated on ice-cooling, recrystallised from water as plates (sublimed above 260°), $[\alpha]_D^{25}$ −33·8° (*c* 0·4 in 5N-hydrochloric acid) (lit.,[13] $[\alpha]_D^{26}$ −35·0°) (Found : C, 61·0; H, 9·65; N, 8·95. Calc. for $C_8H_{15}O_2N$: C, 61·1; H, 9·6; N, 8·9%).

L-α-*Benzamido*-α-cyclo*hexylacetic Acid*.—The mother-liquor separated from the quinine salt of the D-acid was evaporated under reduced pressure to remove most of the alcohol. The residue was acidified with dilute hydrochloric acid and extracted with ether. Evaporation of the dried ethereal extract gave 2·48 g. of crude acid which was extracted with boiling benzene (75 ml.) and filtered from some insoluble material. The solution, on cooling, gave crystals (1·27 g.) of *acid* which on recrystallising from benzene (80 ml.) had m. p. 172—173°, $[\alpha]_D^{23}$ +25·9° (*c* 1·082 in 100 ml. of water containing 4·4 ml. of N-sodium hydroxide) (Found : C, 69·25; H, 7·4; N, 4·95. $C_{15}H_{19}O_3N$ requires C, 68·95; H, 7·3; N, 5·4%). The benzene-insoluble residue above (0·95 g.) was optically inactive and had m. p. 198° undepressed on admixture with DL-α-benzamido-α-*cyclo*hexylacetic acid.

L-2-*Benzylamino*-2-cyclo*hexylethanol*.—A slurry of L-α-benzamido-α-*cyclo*hexylacetic acid (1·88 g.) in dry ether (125 ml.) was added during 10 min. under nitrogen with stirring to lithium aluminium hydride (0·82 g., 3 mols.) in ether (30 ml.). After the initial vigorous reaction the mixture was refluxed for 5 hr., cooled, and decomposed by water (2 ml.). The insoluble material which separated was filtered off and washed with ether. The solid remaining after evaporation of the combined ether solutions was treated with boiling *cyclo*hexane, and the solution, filtered from an insoluble fraction, deposited, on cooling, a small amount of L-2-*benzamido*-2-cyclo*hexylethanol*, m. p. 166°. A mixed m. p. showed that this material was

identical with the *cyclo*hexane-insoluble residue (Found : C, 72·6; H, 8·6; N, 5·9. $C_{15}H_{21}O_2N$ requires C, 72·85; H, 8·6; N, 5·7%). The *cyclo*hexane solution was evaporated and the residue was distilled. The L-*benzylamino-alcohol* boiled at 141°/0·06 mm. (1·17 g.) and had $[\alpha]_D^{23}$ +8·1° (*c* 4·7 in EtOH) (Found : C, 77·3; H, 10·2; N, 5·3. $C_{15}H_{23}ON$ requires C, 77·2; H, 9·9; N, 6·0%) : its *maleate* (from alcohol) had m. p. 172° (Found : C, 65·15; H, 7·8; N, 3·85. $C_{19}H_{27}O_5N$ requires C, 65·3; H, 7·8; N, 4·0%).

L-2-*Amino*-2-cyclo*hexylethanol*.—The benzylamino-compound prepared as above (0·81 g.), dissolved in aqueous alcohol (25%) with hydrated oxalic acid (0·45 g.), was shaken with hydrogen in the presence of 10% palladium–charcoal (1 g.). The residue after evaporation of the filtered solution at reduced pressure was treated with absolute alcohol (20 ml.) and filtered from a small amount of insoluble material. The solution was evaporated to *ca.* 10 ml. and dry ether (100 ml.) was added. The crude oxalate which separated (0·62 g.) was dissolved in water, and the base liberated by the addition of 20% sodium hydroxide solution (10 ml.) was extracted with ether. The ether solution was dried (K_2CO_3) and evaporated, giving the L-*amino-alcohol* which recrystallised from *cyclo*hexane–light petroleum (b. p. 40—60°) had m. p. 74°, $[\alpha]_D^{25}$ +10·4° (*c* 4·4 in EtOH) (Found : C, 67·0; H, 11·9; N, 9·9. $C_8H_{17}ON$ requires C, 67·1; H, 11·9; N, 9·8%). Its *maleate* had m. p. 186—187° (Found : C, 55·9; H, 8·2; N, 5·75. $C_{12}H_{21}O_5N$ requires C, 55·6; H, 8·2; N, 5·4%).

DL-2-*Benzylamino*-2-*phenylethanol*.—α-Benzamido-α-phenylacetic acid (12·75 g.) in a Soxhlet extractor was reduced with lithium aluminium hydride (6·25 g., 3·3 mols.) in ether (250 ml.). After refluxing for 3½ hrs. under nitrogen, the mixture was cooled and decomposed by water (10 ml.), and the solid was filtered off and washed with moist ether (2 × 75 ml.). The combined ether solutions were dried ($MgSO_4$) and evaporated. The residue was recrystallised from light petroleum (b. p. 40—60°), giving the *benzylamino-alcohol*, m. p. 69—70° (8·2 g.) (Found : C, 79·5; H, 7·45; N, 6·05. $C_{15}H_{17}ON$ requires C, 79·25; H, 7·5; N, 6·2%).

L-2-*Benzylamino*-2-*phenylethanol*.—(*a*) L-α-Benzamidophenylacetic acid [16] (1·88 g.) was reduced by the above method with lithium aluminium hydride (0·94 g.) in ether (150 ml.). The *amino-ethanol*, recrystallised from light petroleum (b. p. 40—60°), had m. p. 86° (0·94 g.), $[\alpha]_D^{23}$ +80·0° (*c* 2 in EtOH) (Found : C, 79·7; H, 7·6; N, 5·8%).

(*b*) DL-2-Benzylamino-2-phenylethanol (4·84 g.) and di-*p*-toluoyl-L-tartaric acid [17] were dissolved in boiling 2 : 3 aqueous ethanol (100 ml.). Crystallisation which commenced on cooling was completed in ice. The L-benzylamine di-*p*-toluoyl-L-tartrate (3·6 g.) was obtained as prisms, m. p. 171° (decomp.), by recrystallising the filtered salt from absolute ethanol. This salt (3 g.), suspended in boiling water, was treated with excess of hydrochloric acid, and the mixture cooled and filtered from the precipitated acid. The base liberated with sodium hydroxide and obtained by ether-extraction was purified by dissolving it in light petroleum (b. p. 40—60°, 150 ml.), the solution maintained at 35—40° then being seeded with a crystal of the L-isomer obtained as above. The crystalline product was filtered off at 35—40° and after recrystallising from light petroleum had m. p. 86—87° undepressed on admixture with L-2-benzylamino-2-phenylethanol obtained as in (*a*) and $[\alpha]_D^{25}$ +80° (*c* 2 in EtOH).

L-2-*Amino*-2-*phenylethanol*.—L-2-Benzylamino-2-phenylethanol (0·84 g.) and anhydrous oxalic acid (0·375 g.) in ethanol (60 ml.) and water (15 ml.) were shaken with hydrogen and palladium black (0·2 g.). The theoretical amount was taken up in 5 hr. The catalyst was filtered off, the solution evaporated almost to dryness, and absolute ethanol added. The oxalate which separated was filtered off and recrystallised from ethanol {needles, m. p. 207° (decomp.), $[\alpha]_D^{25}$ −22·9° (*c* 1·7 in H_2O)}. From an aqueous solution of the oxalate, made alkaline with 2N-sodium hydroxide solution and saturated with sodium chloride, the product was obtained by ether-extraction and was recrystallised from benzene–light petroleum (b. p. 40—60°), giving the base, m. p. 77—78°, $[\alpha]_D^{25}$ −27·2° (*c* 9·9 in MeOH) (lit.,[11] m. p. 78—79°, $[\alpha]_D^{17}$ −25·4°) (Found : C, 69·8; H, 7·7; N, 9·9. Calc. for $C_8H_{11}ON$: C, 70·0; H, 8·1; N, 10·2%).

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RESEARCH DIVISION, ALLEN AND HANBURYS LTD.,
WARE, HERTS.

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[16] Minorici, *Chem. Zentr.*, 1920, III, 587.
[17] Stoll and Hofmann, *Helv. Chim. Acta*, 1943, **26**, 922; Hunt, *J.*, 1957, 1926.

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399. *Amine Compounds of the Transition Metals. Part II.*[1] *The Reaction of Niobium Pentachloride with Some Aliphatic Amines.*

By G. W. A. Fowles and C. M. Pleass.

The reaction of niobium pentachloride with dimethylamine at −78° and room temperature, and with mono- and tri-methylamine at room temperature, has been investigated and shown to give $NbCl_3(NMe_2)_2,NHMe_2$, $NbCl_2(NHMe)_3$, and $NbCl_5,2NMe_3$ respectively. In nitrobenzene solution, $NbCl_3(NMe_2)_2,NHMe_2$ has been shown to dissociate into $NbCl_3(NMe_2)_2$ and $NHMe_2$; and $NbCl_2(NHMe)_3$ is found to be largely dimeric. The mechanism of the reactions is discussed.

An investigation of the reaction of transition-metal halides with ammonia has been extended recently [1] to some of the corresponding halide–amine reactions, where the products should be more amenable to structural investigation (*e.g.*, molecular-weight measurements). Fewer hydrogen atoms are directly attached to the nitrogen atom in the amines than in ammonia, and the substances formed should be less polymeric.

For the reaction of niobium pentachloride with ammonia Fowles and Pollard [2] have made a tensimetric study over the temperature range −36° to −63°, and concluded that the overall reaction is given by :

$$NbCl_5 + 4NH_3 \longrightarrow NbCl_3(NH_2)_2 + 2NH_4Cl$$

both the amidochloride and the ammonium chloride taking up loosely held ammonia in addition. There has, however, been no previously reported examination of the reaction of niobium halides with amines, where we would expect some of the halogen atoms to be replaced by amine residues, and in this paper we describe the results of an investigation of the reaction of the pentachloride with mono-, di-, and tri-methylamine.

Experimental

Preparation of Materials.—Niobium pentachloride was prepared by the reaction of dry chlorine on powdered niobium metal (previously treated *in situ* with hydrogen to reduce any oxide) at 400°, and purified by sublimation.[3] It was stored under nitrogen in about 1 g. quantities in sealed tubes, part of the sealed tube consisting of an extended B14 joint. The purity of the chloride was confirmed by analysis (Found : Nb, 34·55; Cl, 66·0. Calc. for $NbCl_5$: Nb, 34·5; Cl, 65·5%).

For the amines see Part I.[1]

Analysis.—The chlorine content was determined by titration with mercuric nitrate solution, with diphenylcarbazone as indicator.[4] Amine was determined by distillation from sodium hydroxide solution into excess of standard hydrochloric acid and back-titration with standard sodium hydroxide to B.D.H. 4·5 indicator. Niobium was determined gravimetrically by precipitation of the tannin complex and subsequent ignition to the pentoxide.[5]

Reaction of Niobium Pentachloride with Dimethylamine.—(*a*) A tube of the chloride was scratched with a glass knife near the tip beyond the greased B14 joint and " hot spotted," and the contents were quickly tipped into the reaction vessel against a countercurrent of dry nitrogen (cf. Part I for details of the apparatus). The apparatus was evacuated by a diffusion pump, and 20—30 c.c. of anhydrous dimethylamine were condensed into the reaction vessel, and the resultant solution was filtered into a second vessel. The extraction with dimethylamine was repeated four times, and the off-white solid remaining in the second vessel after the removal of amine at the pump was extracted with chlorobenzene through a sinter-stick into a third vessel. After the removal of the chlorobenzene from the red-brown solution, a brown

[1] Part I, Fowles and Pleass, *J.*, 1957, 1674.
[2] Fowles and Pollard, *J.*, 1952, 4938.
[3] Alexander and Fairbrother, *J.*, 1949, S223.
[4] Hill, *Chem. and Ind.*, 1954, 852.
[5] Hillebrand, " Applied Inorganic Analysis," Wiley, New York, 2nd Edn., 1953, 603.

solid *product* remained [Found: Nb, 28·35; Cl, 31·7; N, 12·9%; Nb : Cl : N, 1 : 2·93 : 2·95. $NbCl_3(NMe_2)_2,NHMe_2$ requires Nb, 28·0; Cl, 31·0; N, 12·6%].

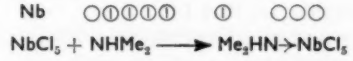
(*b*) Ampoules of chloride and amine were made up (see Part I); as the contents of the ampoule warmed, the pale yellow colour first appearing faded, but at room temperature it reappeared and changed steadily to deep red. After 24 hr. at room temperature, only a trace of crystalline material remained as a residue. The contents of the ampoules were transferred to the reaction vessel, and after the amine had been thoroughly removed at the diffusion pump the residue was extracted with chlorobenzene; removal of the chlorobenzene *in vacuo* at 40° left a brown solid [Found: Nb, 27·2; Cl, 30·2; N, 13·1%; Nb : Cl : N, 1 : 2·91 : 3·13; *M* in nitrobenzene, 171. Calc. for $NbCl_3(NMe_2)_2,NHMe_2$: *M*, 332]. Another solution of the substance in nitrobenzene was warmed to 40°, stirred and evacuated for 1 hr. through a trap cooled in liquid oxygen; a considerable amount of dimethylamine condensed in the trap, and the nitrobenzene solution remained a clear red-brown, the molecular weight of the residual niobium compound being 304 [*M* for $NbCl_3(NMe_2)_2$, 288]. A further run under identical conditions gave *M* 281 after evacuation. The nitrobenzene solutions were examined on a Gouy-type magnetic balance, and the niobium compound was found to be diamagnetic, corresponding to quinquevalent niobium.

Reaction with Monomethylamine.—The reactants were enclosed in ampoules. The chloride dissolved completely in the amine at room temperature to a very pale yellow solution, which gave an almost white product on removal of the amine. Only a small part of this product was dissolved by chlorobenzene, but three extractions at 40° gave a substance whose analysis corresponded to a Nb : Cl : N ratio of 1 : 1·96 : 2·97. Molecular-weight determinations in nitrobenzene solution gave 411 and 443 in successive experiments [Calc. for $NbCl_3(NHMe)_3$: *M*, 254]. The compound was diamagnetic.

Reaction with Trimethylamine.—The ampoule procedure gave a very pale brown solution and a flocculent buff precipitate, but the amine solution contained a negligible amount of solid and extensive extraction of the buff precipitate with trimethylamine did not yield a significant quantity of material; the buff substance was insoluble in the more usual solvents. Direct analysis of this substance after removal of the amine at the pump gave a Nb : Cl ratio of 1 : 5·0 as might be expected, but the Nb : N ratio ranged from 1 : 1·7 to 1 : 2·2.

Discussion

The reaction between niobium pentachloride and dimethylamine at either −78° or room temperature leads to an "amine-solvated" aminobasic chloride $NbCl_3(NMe_2)_2,NHMe_2$. The reaction can be visualised as proceeding through the initial addition of an amine molecule to the pentachloride, the lone pair electrons of the nitrogen atom being donated into a vacant 4*d*-orbital of the niobium atom:



Hydrogen chloride is then split out, by a base-catalysed elimination, leaving $Me_2N{\cdot}NbCl_4$, to which another amine molecule becomes co-ordinated, and so on, leading finally to $NbCl_3(NMe_2)_2,NHMe_2$. It seems likely that a third chlorine atom is not split out because dimethylamino-groups would then occupy three of the five trigonal bipyramidal positions (the same configuration as for niobium pentachloride [6] being assumed) and thereby give rise to considerable steric strain. The observed molecular weight of 171 in nitrobenzene solution is consistent with the dissociation $NbCl_3(NMe_2)_2,NHMe_2 \rightleftharpoons NbCl_3(NMe_2)_2 + NHMe_2$, which gives an average molecular weight of 166 for complete dissociation. This free amine in solution has been removed by warming to 40° and evacuation, and the amine has been trapped and identified. The higher molecular weight of the remaining substance (304, 281) compares well with the predicted value (288) for $NbCl_3(NMe_2)_2$ which would remain in solution. The diamagnetism of the compound shows that there has been no reduction of the niobium to a lower valency state.

[6] Skinner and Sutton, *Trans. Faraday Soc.*, 1940, **36**, 668.

The reaction can then be summarised as :

$$NbCl_5 + 5NHMe_2 = NbCl_3(NMe_2)_2,NHMe_2 + 2NH_2Me_2Cl$$

followed by

$$NbCl_3(NMe_2)_2,NHMe_2 \rightleftharpoons NbCl_3(NMe_2)_2 + NHMe$$

in nitrobenzene.

In the analogous reactions of niobium pentachloride with alcohols and phenols, various workers have succeeded in replacing all five of the chlorine atoms with alkoxy- or phenoxy-residues; [7,8] Funk and Niederlander [9] isolated $NbCl(OPh)_4$ and $NbCl_2(C_{10}H_7O)_3$ from the reaction with phenol and β-naphthol. We should, of course, expect greater replacement with alcohols than with amines, since protons are more readily lost from the initially co-ordinated alcohol molecule; by analogy, hydrolysis of halides is always more extensive than ammonolysis because of the larger ion-product of water.

With monomethylamine, the reaction again undoubtedly involves initial co-ordination of amine molecules to the chloride, followed by the elimination of hydrogen chloride, giving finally $NbCl_2(NHMe)_3$. Reduction of the niobium is again ruled out by the diamagnetism of the product. It seems reasonable to suppose that the replacement of chlorine atoms by methylamino-groups is able to proceed further than with that by the larger dimethylamino-group; there are, moreover, now two replaceable hydrogen atoms in the co-ordinated amine. The molecular weights of **411** and **443** suggest that the molecule is present largely as a dimer, $[NbCl_2(NHMe)_3]_2$ (Required : *M*, 508), although an equilibrium is more probable. Higher polymers may well be present in this original product, although it is unlikely that such compounds would be extracted by the chlorobenzene in the isolation process. The dimerisation is not unexpected, since it enables the niobium atom to achieve an octahedral configuration; a bridging by two methylamino-groups seems more probable than a Nb–Nb link. Bridging by two chlorine atoms, as in Al_2Cl_6 and many platinum and palladium complexes, is of course possible, but it is less likely. Bridging by methylamino-groups may readily arise if the amine initially co-ordinated to one niobium pentachloride molecule takes part with another of the latter in the elimination of hydrogen chloride.

On reaction of trimethylamine with niobium pentachloride the products are unfortunately not separable. It may well be that a simple co-ordination compound $NbCl_5,2NMe_3$ is formed, at least in part, although studies on the formation of alkyls from niobium pentachloride and hydrocarbons, where hydrogen chloride appears to be liberated (see Cotton [10] for a critical review), suggest that some replacement could take place. The overall ratio Nb : Cl : N of approximately 1 : 5 : 2 only tells us that the maximum possible overall replacement must be of one chlorine atom, to give $NbCl_4NMe_2$ plus some chlorinated amine or tetramethylammonium chloride (see Part I).

Reduction to a lower valency state (cf. vanadium; Part I) is rather unlikely since a two-electron change to the tervalent state would be necessary—the quadrivalent state is unstable.

Replacement of chlorine in niobium pentachloride certainly does not proceed further than one stage with trimethylamine, but with dimethylamine two and with monomethylamine three chlorine atoms can be replaced by amine residues in reactions at room temperature. This can be attributed in part to steric requirements and, in part, to the greater ease of removal of hydrogen chloride as more hydrogen atoms are present on the nitrogen.

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THE UNIVERSITY, SOUTHAMPTON. [*Received, December 6th*, 1956.]

[7] Bradley, Chakravati, and Wardlaw, *J.*, 1956, 2381.
[8] Funk and Baumann, *Z. anorg. Chem.*, 1937, **231**, 264.
[9] Funk and Niederländer, *Ber.*, 1928, **61***B*, 249.
[10] Cotton, *Chem. Rev.*, 1955, **55**, 551.

400. *The Heat of Solution of Uranium Tetrachloride and the Hydrolysis of the Uranium*(IV) *Ion.*

By J. A. Hearne and A. G. White.

Measurements have been made of the heat of solution of anhydrous uranium tetrachloride in aqueous hydrochloric acid–lithium chloride mixtures at constant ionic strength. The variation of the heat of solution with hydrochloric acid concentration is in apparent disagreement with current views on the hydrolysis of uranium(IV) and an explanation is offered in terms of the effect of the electrolyte in the solvent on the solvation energy of uranium tetrachloride.

The hydrolysis of quadrivalent uranium in aqueous solution has received little attention. Kraus and Nelson,[1] using a spectrophotometric method, have shown that in acid solutions it is adequately represented by the reaction (*A*), at least down to hydrogen-ion concen-

$$U^{4+} + H_2O \rightleftharpoons UOH^{3+} + H^+ \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (A)$$

trations of the order of 0·01 M. From the variation of the hydrolysis constant, K_H, with temperature these authors calculate a value of 11·7 kcal./mole for the heat-content change, ΔH_H, accompanying reaction (*A*) at infinite dilution. Recently Hietanen [2] has shown that at lower acid concentrations polymeric uranium(IV) species also make an important contribution to the hydrolytic process. The value which she has obtained for K_H is in reasonable agreement with that of the earlier workers.

A direct thermochemical determination of ΔH_H is desirable and, in principle, could be derived from measurements of the heat of solution of anhydrous uranium tetrachloride in aqueous hydrochloric acid–lithium chloride mixtures at constant ionic strength. In such conditions the observed heat of solution $\Delta H_{obs.}$ would be given by eqn. 1, where ΔH_S

$$\Delta H_{obs.} = \Delta H_S + \phi(\Delta H_H) + \psi(\Delta H_C) \quad . \quad . \quad . \quad . \quad . \quad . \quad (1)$$

is the true heat of solution and the functions ϕ and ψ can be derived from the mechanism of the hydrolytic and chloride-ion complex-forming reactions respectively. The inclusion of a term involving ΔH_C, the heat of formation of a chloride-ion complex, is necessary as it has previously been shown [1a,3] that the reaction (*B*) also takes place in aqueous systems.

$$U^4 + Cl^- \rightleftharpoons UCl^{3-} \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (B)$$

Fontana [4] has made a few measurements of the heat of solution of UCl_4 in perchloric acid but these are not sufficiently extensive to yield any reliable conclusions. This paper presents the results of a more systematic series of observations.

Experimental

Uranium tetrachloride was prepared from the pentachloride (kindly provided by Dr. J. K. Dawson of this Division) by heating it in a stream of nitrogen at 500°. The nitrogen was purified by passage over copper heated to 450° and dried by passing through silica gel, magnesium perchlorate, and finally a trap cooled with liquid nitrogen. Thorough drying of the gas stream and apparatus is important and to achieve the latter the preparation vessel was baked out at

[1] Kraus and Nelson, *J. Amer. Chem. Soc.*, (*a*) 1950, **72**, 3901; (*b*) 1955, **77**, 3721.
[2] Hietanen, *Rec. Trav. chim.*, 1956, **75**, 711.
[3] Ahrland and Larsson, *Acta Chem. Scand.*, 1954, **8**, 137.
[4] Fontana, U.S. Atomic Energy Commission Report MDDC 1452 (1947).

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500°, with the dry nitrogen stream flowing, for several hours before loading with UCl_5. The uranium tetrachloride (Found: U, 62·5; Cl, 37·3. Calc. for UCl_4: U, 62·7; Cl, 37·3%; unchanged on vacuum sublimation) was concluded to be not less than 99·6% pure.

All operations with both the pentachloride and tetrachloride were carried out with standard "dry box" techniques. Owing to the extremely hygroscopic nature of these compounds it was found necessary to circulate the air in the dry box slowly through a large trap cooled with liquid oxygen in order to obtain a sufficiently low partial pressure of water in the box.

The calorimetric samples (approx. 20 mg.) were contained in thin-walled glass bulbs, 1 cm. in diameter, which had a small constriction in the neck. The bulbs were weighed in thoroughly dried weighing bottles, which had carefully ground and lightly greased stoppers, returned to the dry box for introduction of the sample, by means of a stainless steel microfunnel, and then reweighed. On return to the box the bulbs were sealed by inserting a glass bead, which rested on the constriction in the neck, placing a small piece of Apiezon W wax above the bead and then melting this, to form a seal around the bead, by means of an electrically heated wire shaped to fit the neck of the bulb. Before use the Apiezon W wax was melted *in vacuo* and maintained at 250—300° for several hours, volatile products being trapped out, in order to prevent any reaction of the sample with volatile materials released when the wax was melted. The efficacy of the bulb-sealing technique was tested by sealing small quantities of P_2O_5 in a number of bulbs and immersing then in water. No change in appearance of the P_2O_5 occurred during 1 yr. All the sample bulbs and microfunnels used were baked *in vacuo* at 350—400° for 6—8 hr. and then transferred to the dry box in an evacuated container. These precautions were necessary to ensure the absence of any appreciable amount of water, for with 20 mg. samples of UCl_4 only 1 mg. of water provides a 1 : 1 molar ratio so that quantities of water of even 100 μg. would greatly affect the heat of solution.

TABLE 1. *Heat of solution of anhydrous* UCl_4 *at* 25·0° *in aqueous* HCl–LiCl *solutions at constant ionic strength,* $\mu = 2·0$. *Final uranium*(IV) *concentration* $\sim 5 \times 10^{-4}$ M.

$[H^+]$	Heat evolved (kcal./mole)	Mean $\Delta H_{obs.}$ (kcal./mole) *	$[H^+]$	Heat evolved (kcal./mole)	Mean $\Delta H_{obs.}$ (kcal./mole) *
2·0	51·31, 51·75	−51·53	0·2	58·65, 58·22, 58·18, 58·06, 58·25, 58·62, 58·18	−58·31 (0·6, ±0·21)
1·6	54·40	−54·40			
1·2	56·10	−56·10	0·1	58·39, 58·22, 58·69	−58·43
1·0	57·00, 56·78	−56·89	0·04	58·50	−58·50
0·6	57·40, 56·90	−57·15	0·02	58·26, 58·55, 58·57	−58·46
0·4	58·42, 58·35, 57·93, 58·03, 57·59, 57·54, 57·52, 58·31, 57·97	−57·96 (0·9, ± 0·33)			

* Numerals in parentheses are the range in ΔH followed by the standard deviation, σ.

The calorimetric equipment used was a modification of that previously described.[5] The volume of the calorimeter was 130 ml., and 100 ml. quantities of solvent were used for each run. The stirrer and glass tubes containing the thermistor and heater were replaced by components made from platinum and the sample-carrying and -breaking mechanism was replaced by a tungsten rod which ended a little above the calorimeter and carried on its lower end a short section of Perspex rod (to prevent rapid heat conduction) followed by a length of platinum rod the end of which fitted into the neck of the sample bulb. The sample bulbs were fixed to the platinum rod with Apiezon W wax and were broken by depressing them on a small platinum platform carrying three stout spikes. The platform was suspended from the Polythene plug closing the calorimeter by platinum tubing.

The solvent was prepared by mixing appropriate amounts of 2M stock solutions of hydrochloric acid and lithium chloride.

Results.—The values obtained for the heat of solution of uranium tetrachloride are presented in Table 1 and the mean values of $\Delta H_{obs.}$ are plotted as a function of $\log_{10}[H^+]$ in Fig. 1. The two series of measurements at $[H^+] = 0·4$ and 0·2 were carried out to determine the overall reproducibility of the results and from these it would seem reasonable to assign a standard deviation of ±0·33 kcal./mole to the values of $\Delta H_{obs.}$.

[5] Hutchinson and White, *J. Sci. Instr.*, 1955, **32**, 309.

Discussion

If current views on the mechanism of hydrolysis of uranium(IV) in acid solutions and of the formation of a chloride-ion complex [1,2,3] are accepted then the functions ϕ and ψ of eqn. 1 are

$$\phi = \frac{[UOH^{3+}]}{[U^{IV}]}\Delta H_H \text{ and } \psi = \frac{[UCl^{3+}]}{[U^{IV}]}\Delta H_C$$

where $[U^{IV}]$ is the total analytical concentration of uranium(IV).

Now $$[UOH^{3+}] = \frac{K_H[U^{4+}]}{[H^+]} \; ; \; [UCl^{3+}] = K_c[U^{4+}][Cl^-]$$

where K_c is the equilibrium constant for the formation of the UCl^{3+} ion, and

$$[U^{IV}] = [U^{4+}] + [UOH^{3+}] + [UCl^{3+}]$$

from which $$[U^{4+}] = [U^{IV}]/(1 + K_H/[H^+] + K_c[Cl^-])$$

When the appropriate substitutions are made for ϕ and ψ, equation 1 becomes

$$\Delta H_{obs.} = \Delta H_S + \frac{K_H}{K_H + [H^+](1 + K_c[Cl^-])}\Delta H_H + \frac{K_c[Cl^-]}{1 + K_c[Cl^-] + K_H/[H^+]}\Delta H_c \quad (2)$$

In order to make use of eqn. (2) it is necessary to know ΔH_S, ΔH_C, K_H, and K_c in addition to the hydrogen-ion and chloride-ion concentrations. Of these quantities ΔH_H and K_H are given by Kraus and Nelson [1] and K_c can also be calculated from these authors' data. A value of K_c, at ionic strength $\mu = 1{\cdot}0$, is also given by Ahrland and Larsson [3] but in view of their technique, which depends upon an accurate knowledge of complex-formation between chloride ion and the uranyl ion, the value is probably less reliable than those obtained from the former workers' results. Fontana [4] has measured the heat of solution of UCl_4 in 2M-$HClO_4$ and finds $\Delta H_{obs.} = -53{\cdot}62$ kcal./mole. This value, together with that given in our Experimental section for 2M-HCl, can be used with the known constants to derive ΔH_c from eqn. 2. With $K_c = 0{\cdot}27$ at $\mu = 2{\cdot}0$ (estimated from the data of Kraus and Nelson [1]), $\Delta H_H = 11{\cdot}0$ kcal./mole, and $K_H = 0{\cdot}0236$ at $\mu = 2{\cdot}0$, the value obtained for ΔH_c is 6·2 kcal./mole.

The second and the third term of eqn. 2 have been computed, this set of values being used for the constants, and ΔH_S has been chosen to make eqn. (2) coincide with the experimental $\Delta H_{obs.}$ at $[H^+] = 2{\cdot}0$M. The values of $\Delta H_{obs.}$ which result are plotted against $\log_{10}[H^+]$ in the Figure, from which it is evident that a considerable divergence exists between the experimental and calculated curves. The calculated values of $\Delta H_{obs.}$ are almost unchanged from hydrogen-ion concentrations of 2·0—0·5M and below this steadily become more positive, while from 2·0 to 0·5M the experimental results become rapidly more negative and thereafter are almost constant.

In seeking an explanation of this anomaly two major possibilities must be considered, namely, (1) that (*A*) does not correctly represent the course of hydrolysis, and (2) that eqn. (2) does not express the observed heat of solution accurately. The weight of evidence available is such as to leave no doubt that the first of these possibilities can be excluded. In particular it is certain [1b] that ΔH_H must be positive and not, as the experimental values of $\Delta H_{obs.}$ seem to imply, negative. Further, to obtain even approximate agreement between calculated and experimental values of $\Delta H_{obs.}$ not only would a negative value of ΔH_H be required, but it would be necessary to postulate the occurrence of a hydrolytic reaction (*C*)

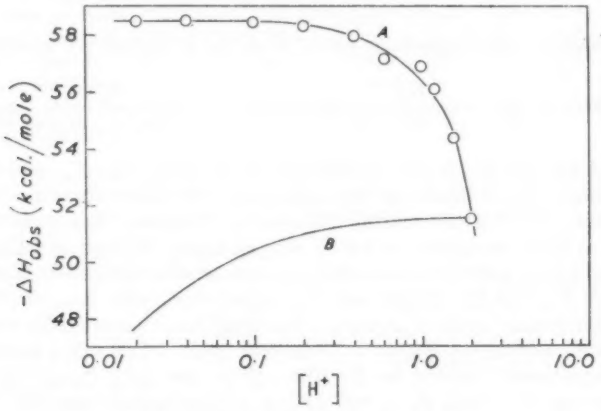
$$U^{4+} + nH_2O \rightleftharpoons U(OH)_n^{(4-n)+} + nH^+ \quad . \; . \; . \; . \; . \; (C)$$

XUM

with values of n between 2 and 3; Kraus and Nelson [1a] have confirmed that when anhydrous UCl_4 is dissolved in aqueous acid solutions n is always less than unity. The good agreement between the values of K_{II} determined by these authors and by Hietanen,[2] who used an entirely different experimental technique, is also very strong support for the correctness of their views.

These considerations suggest that an explanation must be sought in the second possibility. Equation (2) can be inadequate for only two reasons: there may be other reactions occurring which have not been considered in its derivation, and the true heat of solution ΔH_S may be a function of the composition of the solvent medium and not, as was tacitly assumed, a constant. In the system under consideration the only additional reactions which could occur are the polymerisation of the hydrolysed uranium ions and the oxidation of U^{IV} to U^{VI} by dissolved oxygen. Polymerisation is unlikely to be important under these conditions as it is markedly retarded by hydrogen ions and the

Heat of solution of uranium tetrachloride in hydrochloric acid–lithium chloride mixtures at 25° (μ = 2·0).



A, Experimental. *B*, Calc. from eqn. (2).

temperature–time plots of the calorimetric measurements showed no abnormalities which could be attributed to a slow thermal process. To determine the extent of oxidation experiments were carried out in which 20 mg. of UCl_4 were dissolved in 100 ml. of HCl–LiCl mixtures and then stirred, in air, for 15—20 min. (*i.e.*, for approximately the same length of time as a calorimetric measurement required) after which the U^{IV} content of the solution was determined. The results obtained were ratios of U^{IV} to total uranium of 0·996 and 1·002 at hydrogen-ion concentrations 2·0 and 0·2 respectively, and it is clear that no oxidation can have occurred. The only remaining explanation of the discrepancy is that ΔH_S is markedly dependent on the composition of the solvent.

A number of factors contribute to ΔH_S; the lattice energy of the crystal, the heats of solvation of the positive and negative ions and the heat of dilution of the solution. Of these the heat of dilution will certainly depend on the nature of the medium, but its contribution to ΔH_S is a minor one (20% variations in the weight of UCl_4 used have no detectable effect on $\Delta H_{obs.}$) and in a medium of constant ionic strength it would be expected to be almost constant. The lattice energy is a function only of the solid material and will be entirely independent of the solvent; but in recent years evidence has been accumulating which shows that the heats of solvation of ions are quite markedly affected by the presence

of other electrolytes in the solvent.[6,7,8] None of these investigations has been carried out at constant ionic strength but the work of Samoilov [8] indicates that the hydrogen ion causes a particularly large effect, one observation which has an important bearing on the present work being that at equivalent concentrations the heat of solution of NaCl is depressed more strongly by hydrochloric acid than by lithium chloride. In all the salts studied (LiCl, NaCl, KCl, $MgCl_2$, $CaCl_2$) the heat of solution becomes more endothermic on addition of hydrochloric acid to the solvent, the effect being linearly related to its concentration. Klemm [6] has examined the data available for $AlCl_3$, $GaCl_3$, $InCl_3$, $LaCl_3$, and $FeCl_3$ and has shown that in all cases the addition of a given amount of hydrochloric acid to the solvent produces approximately the same change in $\Delta H_{obs.}$. In these cases the relation between $\Delta H_{obs.}$ and HCl concentration is not linear but is roughly parallel to that found for uranium tetrachloride in the present work as are the results for $ThCl_4$ [9] and $PuCl_3$.[10] To account for these results Klemm suggests that they reflect the formation of chloride ion complexes, the process being considered to be highly endothermic owing to the strong binding between chloride ion and water. This explanation however, as the present results show, can be only partly true. At a constant total chloride-ion concentration and constant ionic strength no explanation based solely on chloride-complex formation could account for the large change in $\Delta H_{obs.}$ with change in hydrogen-ion concentration and as this cannot be due to hydrolysis then it is clear that the positive ions must have a special effect on the heat of hydration, that of the hydrogen ion being much greater than that of lithium ion, in agreement with Samoilov's finding.[8]

The heat of solution of UCl_4 in 0·5M-perchloric acid (−55·6 kcal./mole) and in 0·1M-$HClO_4$ + 0·4M-$LiClO_4$ (−54·2 kcal./mole) has been measured by Fontana [4] and it will be noticed that the change in $\Delta H_{obs.}$ is in the direction predicted by eqn. (2) and opposite to that found in 2M-HCl–LiCl mixtures at these acid concentrations. This difference in behaviour is undoubtedly related to the difference in ionic strength in the two sets of measurements, a lower ionic strength leading to a smaller effect of hydrogen-ion concentration on ΔH_S. It is possible to use these results, in combination with equation (2), to calculate a value for ΔH_H and by using the constants given previously a figure of 8·3 kcal./mole is obtained. This value is less than that found by Kraus and Nelson [1b] but this is to be expected as the change from 0·1M to 0·5M acid will not only alter the second term in eqn.(2) but will also make ΔH_S more positive, thus making the overall difference in $\Delta H_{obs.}$ less than that required by the hydrolytic process alone. It is apparent that any attempt to derive heats of hydrolysis from measurements of heats of solution is liable to be seriously misleading unless adequate data are available from which the effect of the medium on the heats of solvation of the ions can be evaluated.

CHEMISTRY DIVISION, A.E.R.E., HARWELL, DIDCOT, BERKS. [*Received, December 7th*, 1956.]

[6] Klemm, *Z. anorg. Chem.*, 1942, **249**, 23.
[7] Voskresenskaya and Ponomareva, *Zhur. fiz. Khim.*, 1946, **20**, 433; Samoilov, *Izvest Akad. Nauk S.S.S.R., Otdel. khim. Nauk*, 1952, 627; Kaganovich and Mishchenko, *Doklady Akad. Nauk. S.S.S.R.*, 1952, **87**, 89.
[8] Samoilov, *Doklady Akad. Nauk, S.S.S.R.*, 1951, **81**, 641.
[9] Westrum and Robinson, Paper 6.50, "The Transuranium Elements," Vol. 14*B*, National Nuclear Energy Series, McGraw-Hill, New York, 1949.
[10] *Idem, ibid.*, Paper 6.54.

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401. *The Thermal Decomposition of Tetrafluoroethylene.*

By B. Atkinson and V. A. Atkinson.

The thermal decomposition of systems derived from tetrafluoroethylene, occurring in a nickel vessel at temperatures from 550° to 750°, is described.

The tetrafluoroethylene–perfluoro*cyclo*butane equilibrium mixture decomposes at temperatures above 550° forming perfluoropropene by a first-order mechanism. This in turn decomposes giving perfluoro*iso*butene in a reaction with an order of 1·5. A reaction scheme, based on the difluoromethylene radical as intermediate, is shown to be in accord with the experimental results.

At temperatures above 700° perfluoro*iso*butene is shown to disproportionate giving perfluoroethane and various non-volatile products by a first-order mechanism. A reaction scheme, based on the trifluoromethyl radical, is suggested.

Results reported by Miller [1] and Atkinson and Trenwith [2] show that the thermal decomposition of tetrafluoroethylene can be divided into three phases. At low temperatures perfluoro*cyclo*butane is the main product; at medium temperatures perfluoropropene and a perfluorobutene are produced; and at high temperatures perfluoroethane is formed.

Atkinson and Trenwith also performed a detailed investigation between 300° and 590°, showing that a reversible cyclic dimerisation occurs :

$$2CF_2{:}CF_2 \longrightarrow (CF_2)_4,\ k_1 = 10{\cdot}3 \times 10^7 \exp(-25{,}400/\boldsymbol{R}T)\ \text{l. mole}^{-1}\ \text{sec.}^{-1} \quad . \quad (1)$$

$$(CF_2)_4 \longrightarrow 2CF_2{:}CF_2,\ k_2 = 8{\cdot}9 \times 10^{15} \exp(-74{,}100/\boldsymbol{R}T)\ \text{sec.}^{-1} \quad . \quad . \quad (2)$$

Their values for rate constants are substantially in agreement with those of Lacher, Tompkin, and Park [3] for reaction (1) and those of Gray and Pritchard [4] for reaction (2). No detailed investigation of the formation of perfluoropropene, perfluorobutene, and perfluoroethane has hitherto been made.

The work of Brice *et al.*[5] has proved that the perfluorobutene produced was perfluoro-*iso*butene and not perfluorobut-1-ene as Miller, and Atkinson and Trenwith, had assumed.

Experimental

Materials.—(a) *Tetrafluoroethylene.* The gas, from a small cylinder, was first stored over water to remove hydrogen chloride and then fractionated in a low-temperature (Podbielniak) distillation column. Its purity was checked by its infrared spectrum.

(b) *Perfluoroethane, perfluoropropene, perfluoro*cyclo*butane, and perfluoro*iso*butene.* The products of several pyrolyses, performed under conditions appropriate for the production of the required material, were amalgamated and that material was fractionally distilled. A second fractionation was performed to purify the material, and the purity was checked by infrared spectroscopy.

Pyrolyses of Fluorocarbons.—(a) *Apparatus.* All pyrolyses were performed by static methods. The gas to be pyrolysed was introduced into a cylindrical (10 in. long, 2 in. o.d.) reaction vessel set in a horizontal tubular wire-wound furnace with an electronic control of the type described by Roberts,[6] which kept the temperature constant to within ±0·5°. The temperature of the reaction vessel was measured by a chromel–alumel thermocouple in a coaxial well traversing almost the entire length of the reaction vessel. The capillary inlet tube was connected to a capillary manometer, by which changes in total pressure were followed to

[1] Miller, "Preparation and Technology of Fluorine and Organic Fluorine Compounds," National Nuclear Energy Series, Vol. VII, 1951, chap. 32.
[2] Atkinson and Trenwith, *J.*, 1953, 2082.
[3] Lacher, Tompkin, and Park, *J. Amer. Chem. Soc.*, 1952, **74**, 1693.
[4] Gray and Pritchard, *J.*, 1956, 1002.
[5] Brice, La Zerte, Hals, and Pearlson, *J. Amer. Chem. Soc.*, 1953, **75**, 2698.
[6] Roberts, *Electronic Engineering*, 1951, **23**, 51.

the nearest 0·5 mm. Reaction vessels of stainless steel (En. 58B) and nickel were used. Since oxide scale was shown to interfere with the pyrolyses, the steel vessel was welded by the argon-arc technique to minimise scaling, and both the steel and the nickel vessels were filled with tetrafluoroethylene and left at 650° overnight to remove any traces of oxide formed during welding.

(b) *Procedure.* A series of pyrolyses with a common initial reactant pressure were performed at a given temperature, and each member was terminated after a different time. The volatile materials in the system were measured by infrared methods.

Infrared Analysis.—A Grubb–Parsons double-beam spectrometer was used and calibration curves for each pure standard gas were drawn.

Trace compounds, when suspected, were characterised by amalgamating the products of several identical pyrolyses, performing a fractionation, and subjecting suspect fractions to infrared analysis. The identities of these compounds were established by reference to either Brice *et al.*[5] or the American Petroleum Institute " Catalog of Infra-Red Spectral Data," where the established spectra of all the fluorocarbon gases likely to be encountered are recorded. These sources were also used to show which lines could be used for the estimation of each product.

Perfluoro*cyclo*propane and perfluorobut-1-ene (uniquely characteristic lines at 11·6 μ and 10·6 μ respectively) were never encountered. Perfluorobut-2-ene (uniquely characteristic line at 11·3 μ) was found in traces. Carbon tetrafluoride and perfluoropropane share a characteristic line at 7·9 μ. Both compounds appear as minute traces, perfluoropropane being produced at medium temperatures and carbon tetrafluoride at high temperatures.

Tetrafluoroethylene, perfluoroethane, perfluoropropene, perfluoro*cyclo*butane, and perfluoro-*iso*butene were the most important compounds in the pyrolyses investigated, comprising over 99% of the volatile materials analysed in each case. Of these, perfluoro*cyclo*butane and perfluoro*iso*butene had uniquely characteristic lines at 10·45 μ and 10·05 μ respectively. The line at 5·6 μ was used for the estimation of perfluoropropene, because the only other compound which it characterised, perfluorobut-1-ene, was never detected in the system. The triplet at 9·0 μ had to be used for the estimation of perfluoroethane, although the trace products carbon tetrafluoride and perfluorobut-2-ene also had lines in this region. All the above lines had distinct resolution, free from overlap by the lines of other of the major products, and the compounds could be estimated to within 1%.

The 8·45 μ line used for the estimation of the parent compound, tetrafluoroethylene, was the least satisfactory since it overlapped the 8·4 μ line of perfluoro*iso*butene and the 8·5 μ line of perfluoropropene, both major products. The extrapolation necessary in the estimation of tetrafluoroethylene reduced the accuracy to ±5%. Fortunately, it transpired that although tetrafluoroethylene was an important intermediate at medium temperature, it was not necessary to base any detailed calculations on the variation of the tetrafluoroethylene pressure.

Results

Pyrolyses in Nickel.—Homogeneous gas-phase reactions occurred. Figs. 1 and 2 show the results obtained from the pyrolyses of tetrafluoroethylene and perfluoro*cyclo*butane at 650° and 700° respectively. They show that four reactions successively produce perfluoro*cyclo*butane, perfluoropropene, perfluoro*iso*butene, and perfluoroethane from tetrafluoroethylene.

Low-temperature phase. The first reaction in the series, that producing perfluoro*cyclo*butane, occurs at temperatures above 300° and has been adequately investigated by Atkinson and Trenwith.[3] The results obtained for pyrolyses at temperatures above 550° substantially confirm their conclusions.

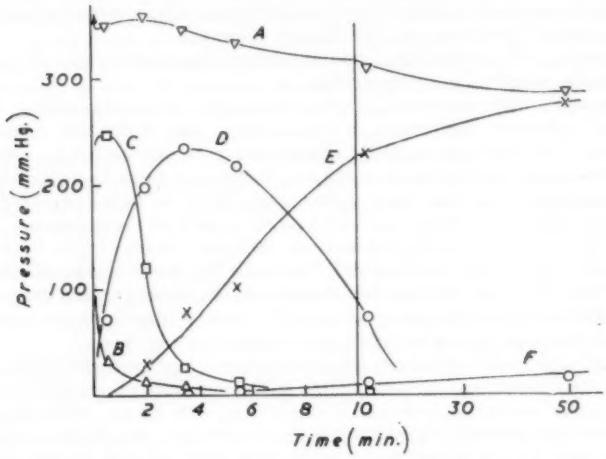
Medium-temperature phase. Fig. 1 clearly shows that the second reaction is that producing perfluoropropene, and not the perfluorobutene as Trenwith [7] suggests. The reactant is evidently the tetrafluoroethylene–perfluoro*cyclo*butane equilibrium mixture produced quickly by reactions (1) and (2), so it was investigated with each of these compounds as starting material. Series of pyrolyses of tetrafluoroethylene were performed at 600° and 650° and of perfluoro*cyclo*butane at 550°, 575°, 600°, and 650° (see Figs. 1, 2, and 3). The results from the two series performed at 600° were identical. Graphs of log $d[C_4F_8]/dt$ against log $[C_4F_8]$ showed the reaction to be of the first order in perfluoro*cyclo*butane.

Fig. 1 also shows that perfluoro*iso*butene is not produced until an appreciable quantity of

[7] Trenwith, Ph.D. Thesis, London, 1952.

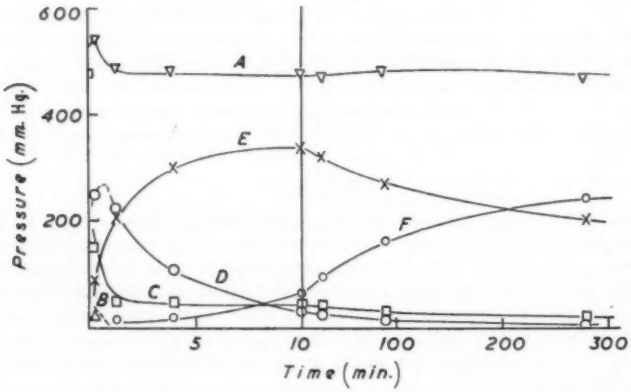
perfluoropropene has been formed. It was therefore assumed that the bulk of the *iso*butene was formed from the propene. The reaction producing perfluoro*iso*butene was therefore investigated by pyrolysing perfluoropropene at 600°, 625°, 650°, and 675° (Fig. 4). It was found

FIG. 1. *Pyrolysis of tetrafluoroethylene at* 650°.



A, Total pressure; *B*, tetrafluoroethylene; *C*, perfluoro*cyclo*butane; *D*, perfluoropropene; *E*, perfluoro*iso*butene; *F*, perfluoroethane.

FIG. 2. *Pyrolysis of perfluoro*cyclo*butane at* 700°.



A, Total pressure; *B*, tetrafluoroethylene; *C*, perfluoro*cyclo*butane; *D*, perfluoropropene; *E*, perfluoro*iso*butene; *F*, perfluoroethane.

that the reaction had an order of 1·5. Certain small material losses were noted. It is suggested that these might be associated with a white dust that settled in the cooler parts of the system.

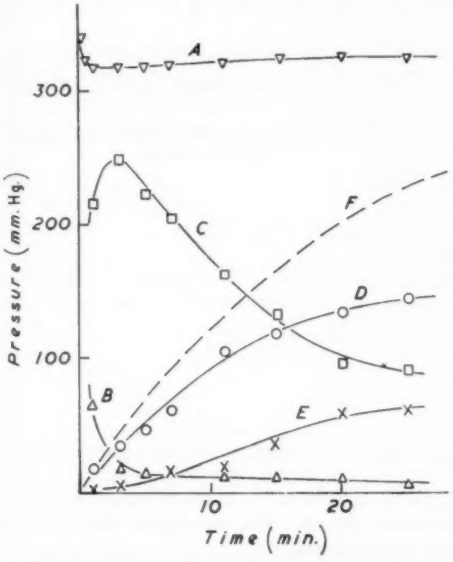
High-temperature phase. Fig. 2 clearly shows that the perfluoroethane is formed at 700° when the only major reactant is perfluoro*iso*butene. It is therefore assumed that most, if not all, of the perfluoroethane is produced from perfluoro*iso*butene. The pyrolysis of perfluoro*iso*-butene at 700°, 725°, and 750° was investigated (see Fig. 5). The reaction was found to be of the first order.

During these pyrolyses the total pressure remained virtually constant (see Fig. 5) showing that the overall reaction must have been :

$$(CF_3)_2C{:}CF_2 \longrightarrow CF_3{\cdot}CF_3 + \text{non-volatile materials} \quad . \quad . \quad . \quad . \quad . \quad (3)$$

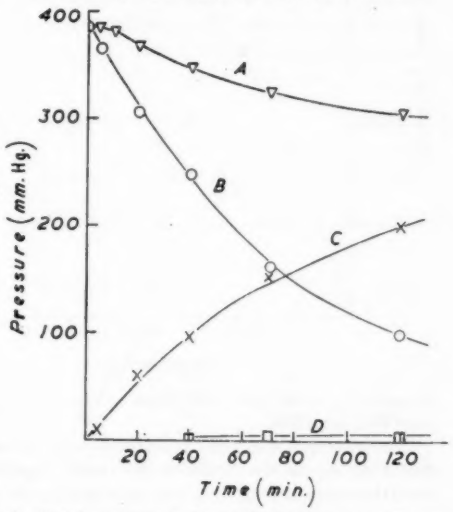
The non-volatile materials proved separable into grey and dark-red solids. Organic microanalysis showed that both solids had approximate formulæ C_5F_4. Since the overall composition of the non-volatile materials in equation (3) should be CF, a certain amount of fluorine may have been lost by reaction with the nickel vessel. The dark-red solid was insoluble in water, but readily soluble in organic solvents. It absorbed heavily in the blue and ultraviolet regions, as does perfluorobutadiene.[8] The infrared spectrum of the red solid was generally indeterminate

FIG. 3. *Pyrolysis of tetrafluoroethylene at* 600°.



A, Total pressure; *B*, tetrafluoroethylene; *C*, perfluoro*cyclo*butane; *D*, perfluoropropene; *E*, perfluoro*iso*butene; *F*, calculated pressure of perfluoropropene if no decomposition to perfluoro*iso*butene.

FIG. 4. *Pyrolysis of perfluoropropene at* 600°.



A, Total pressure; *B*, perfluoropropene; *C*, perfluoro*iso*butene; *D*, octafluoro*cyclo*butane.

but a sharp peak at 5·75 μ was ascribed to the fluorocarbon C:C double bond. The line characteristic of this bond is found at 5·56 μ in the perfluoroalk-1-enes and shifts to higher wavelengths for conjugated compounds (*e.g.*, 5·65 for perfluorobutadiene [8]). It was concluded that the red solid was a complex mixture of highly conjugated unsaturated fluorocarbons of relatively high molecular weight. The grey solid, insoluble in all common reagents, was probably a mixture of elementary carbon and some high-molecular weight fluorocarbon. It is thought to represent the final degradation product of the conjugated compounds.

Pyrolyses in Stainless Steel.—The pyrolysis of tetrafluoroethylene or perfluoro*cyclo*butane in steel resulted, after the establishment of the equilibrium between tetrafluoroethylene and octafluoro*cyclo*butane, in a slowly decelerating pressure decrease virtually to zero. This was just noticeable in pyrolyses at 600°, but quite appreciable at 650°. Analysis of the volatile matter involved showed that perfluoropropene and perfluoro*iso*butene were being formed, just as with similar pyrolyses in the nickel vessel.

The pyrolyses of perfluoropropene and perfluoro*iso*butene in steel resulted in the same pressure decrease virtually to zero, occurring at appreciable rates at temperatures as low as

[8] Haszeldine, *J.*, 1952, 4423.

450°. The rate of the reaction was not reproducible; successive runs became slower and slower unless the steel vessel was evacuated at 800° for several hours between each run.

The products of these pyrolyses were grey-black flakes whose organo-carbon content was 98% carbon. The inorganic content, soluble in dilute hydrochloric acid, was fluorides of

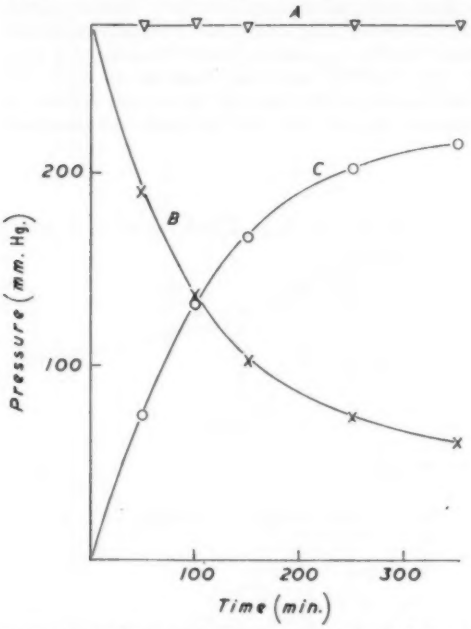


FIG. 5. *Pyrolysis of perfluoroisobutene at* 725°.

A, Total pressure; *B*, perfluoro*iso*butene; *C*, perfluoroethane.

manganese, iron, and chromium. The nickel and titanium components of the stainless steel were not attacked.

The reaction was thus a heterogeneous attack on the steel vessel. The carbon and fluoride coat forming on the walls of the vessel impeded further attack. The peeling-off of this coat (and therefore the attack) was accelerated by high temperatures.

DISCUSSION

The Reaction producing Perfluoropropene.—It is desirable to consider a reaction scheme that would cover the first-order reaction producing perfluoropropene from the tetrafluoroethylene–perfluoro*cyclo*butane equilibrium mixture. The reaction scheme now suggested is based on difluoromethylene because this radical is known to exist [9] and reaction schemes based on other radicals would be expected to produce appreciable quantities of saturated compounds, for which there is no experimental evidence.

Tetrafluoroethylene and perfluoro*cyclo*butane are both possible reactants; it is possible to derive two alternative schemes for the two possible reactants that fit the kinetic evidence recorded above.

In the first scheme perfluoropropene and difluoromethylene are formed by the dissociation of perfluoro*cyclo*butane :

$$2CF_2{:}CF_2 \longrightarrow (CF_2)_4 \quad (1)$$

$$(CF_2)_4 \longrightarrow 2CF_2{:}CF_2 \quad (2)$$

$$(CF_2)_4 \longrightarrow CF_3{\cdot}CF{:}CF_2 + CF_2 \quad (4)$$

$$CF_2 + CF_2{:}CF_2 \longrightarrow CF_3{\cdot}CF{:}CF_2 \quad (5)$$

$$CF_3{\cdot}CF{:}CF_2 \longrightarrow CF_2{:}CF_2 + CF_2 \quad (6)$$

[9] Atkinson, *J.*, 1952, 2684.

If it is assumed that a stationary state is attained where the difluoromethylene concentration is constant, then,

$$k_4[(CF_2)_4] = k_5[CF_2][C_2F_4] - k_6[CF_3{\cdot}CF{:}CF_2] \quad . \quad . \quad . \quad . \quad . \quad (7)$$

and, if k_6 is small,

$$d[CF_3{\cdot}CF{:}CF_2]/dt = 2k_4[(CF_2)_4] \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (8)$$

Also,

$$4d[(CF_2)_4]/dt + 2d[C_2F_4]/dt = -3d[CF_3{\cdot}CF{:}CF_2]/dt \quad . \quad . \quad . \quad (9)$$

whence

$$2d[(CF_2)_4]/dt + d[C_2F_4]/dt = -3k_4[(CF_2)_4] \quad . \quad . \quad . \quad . \quad . \quad (10)$$

$$2 \ln [(CF_2)_4] + \int\{d[C_2F_4]/[(CF_2)_4]\} = 3k_4t + \text{Constant} \quad . \quad . \quad . \quad (11)$$

In order to proceed further with this fundamental equation it is necessary to make the further assumption that the basic tetrafluoroethylene–perfluoro*cyclo*butane equilibrium is attained rapidly compared with subsequent reactions, and that these subsequent reactions do not greatly disturb the equilibrium, *i.e.*, that

$$k_1[C_2F_4]^2 = k_2[(CF_2)_4] \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (12)$$

whence

$$2 \ln [(CF_2)_4] - (k_2/\{k_1[(CF_2)_4]\})^{\frac{1}{2}} = -3k_4t + \text{Constant} \quad . \quad . \quad . \quad (13)$$

Table 1 shows values of k_4 derived from equations (8) and (13). From these values the following Arrhenius equation was derived

$$k_4 = 3{\cdot}9 \times 10^{16} \exp(-79{,}000/\boldsymbol{R}T) \text{ sec.}^{-1}. \quad . \quad . \quad . \quad . \quad . \quad (14)$$

TABLE 1.

Temperature	550°	575°	600°	625°	650°
10^6k_4 (sec.$^{-1}$) from eqn. (8)	50	200	633	2960	8570
10^6k_4 (sec.$^{-1}$) from eqn. (13)	60	260	660	4000	9440

A second scheme based on the association of two tetrafluoroethylene molecules is equally likely on kinetic grounds:

$$2CF_2{:}CF_2 \longrightarrow (CF_2)_4 \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (1)$$

$$(CF_2)_4 \longrightarrow 2CF_2{:}CF_2 \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (2)$$

$$2CF_2{:}CF_2 \longrightarrow CF_3{\cdot}CF{:}CF_2 + CF_2; \; d[C_2F_4]dt = -k_{15}[C_2F_4]^2 \quad . \quad (15)$$

$$CF_2 + CF_2{:}CF_2 \longrightarrow CF_3{\cdot}CF{:}CF_2 \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (5)$$

$$CF_3{\cdot}CF{:}CF_2 \longrightarrow CF_2{:}CF_2 + CF_2 \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (6)$$

If this is treated exactly as the previous scheme, it is possible to derive

$$d[CF_3{\cdot}CF{:}CF_2]/dt = [(CF_2)_4]k_{15}k_2/k_1 \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (16)$$

and

$$2 \ln [(CF_2)_4] - (k_2/k_1[(CF_2)_4])^{\frac{1}{2}} = -1{\cdot}5 \; k_{15}k_2t/k_1 + \text{constant} \quad . \quad . \quad (17)$$

By comparison with eqns. (8) and (13) it can be seen that

$$k_{15} = 2k_1k_4/k_2 \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (18)$$

From equations (1), (2), (14), and (18) it can be calculated that

$$k_{15} = 9{\cdot}0 \times 10^8 \exp(-30{,}300/\boldsymbol{R}T) \text{ l. mole}^{-1} \text{ sec.}^{-1} \quad . \quad . \quad . \quad (19)$$

It is possible to adjudicate between the two schemes outlined above by considering the circumstances at 500°. It can be calculated that at 500° and 400 mm.

$$\text{Rate (1)} = 4{\cdot}7 \times 10^{-4} \text{ mole l.}^{-1} \text{ sec.}^{-1} \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (20)$$

$$\text{Rate (2)} = 8{\cdot}3 \times 10^{-8} \text{ mole l.}^{-1} \text{ sec.}^{-1} \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (21)$$

$$\text{Rate (4)} = 1{\cdot}5 \times 10^{-8} \text{ mole l.}^{-1} \text{ sec.}^{-1} \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (22)$$

$$\text{Rate (15)} = 1{\cdot}7 \times 10^{-4} \text{ mole l.}^{-1} \text{ sec.}^{-1} \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (23)$$

If reaction (4) represents the true reaction path then the pyrolysis of tetrafluoroethylene at 500° should yield little or no perfluoropropene, because not only is (4) the slowest reaction, but it must await the build-up of perfluoro*cyclo*butane by reaction (1) before it can commence. If reaction (15) is correct, then the pyrolysis of tetrafluoroethylene at 500° should readily yield perfluoropropene since reaction (1) is only about three times as fast as reaction (15). Tetrafluoroethylene at 430 mm. pressure was pyrolysed for 20 sec. at 500°. No perfluoropropene was found when the products were subjected to infrared analysis; they contained 38·5% of perfluoro*cyclo*butane, which corresponds to dimerisation of 55·5% of the original tetrafluoroethylene. If the second reaction scheme, involving reaction (15), were the true reaction path for formation of perfluoropropene, about 15% of this compound would have been found in the products. It is concluded that the first scheme, involving reaction (4), represents the true reaction path.

The Reaction producing Perfluoroisobutene.—Any reaction scheme put forward has to explain (*a*) the production of perfluoro*iso*butene from perfluoropropene by a reaction of order 1·5 and (*b*) the existence of an apparent induction period in the total-pressure curve; the initial rate was less than the maximum rate (Fig. 4). The ready production of perfluoro-*iso*butene with perfluoropropene from perfluoro*cyclo*butane or tetrafluoroethylene (Fig. 3) suggests that the intermediates in both pyrolyses are identical. Further evidence for this supposition was found in that the pyrolysis of pure perfluoropropene at 600° for 40 minutes or more produced detectable quantities (about 1%) of perfluoro*cyclo*butane, which must have been in equilibrium with tetrafluoroethylene and difluoromethylene by reactions (2) and (4). Accordingly the following mechanism involving tetrafluoroethylene and difluoromethylene was derived:

$$CF_3{\cdot}CF{:}CF_2 \longrightarrow CF_2{:}CF_2 + CF_2 \quad . \quad . \quad . \quad . \quad . \quad . \quad (6)$$

$$CF_2{:}CF_2 + CF_2 \longrightarrow CF_3{\cdot}CF{:}CF_2 \quad . \quad . \quad . \quad . \quad . \quad . \quad (5)$$

$$CF_2 + CF_3{\cdot}CF{:}CF_2 \longrightarrow (CF_3)_2C{:}CF_2 \quad . \quad . \quad . \quad . \quad . \quad . \quad (24)$$

$$CF_2{:}CF_2 + CF_3{\cdot}CF{:}CF_2 \longrightarrow (CF_3)_2C{:}CF_2 + CF_2 \quad . \quad . \quad . \quad . \quad (25)$$

If it is assumed that a steady state is obtained at which the difluoromethylene and tetrafluoroethylene concentrations are constant, then

$$k_6[CF_3{\cdot}CF{:}CF_2] + k_{25}[C_2F_4][CF_3{\cdot}CF{:}CF_2] = k_5[C_2F_4][CF_2] + k_{24}[CF_3{\cdot}CF{:}CF_2][CF_2] \quad . \quad (26)$$

$$k_6[CF_3{\cdot}CF{:}CF_2] = k_5[C_2F_4][CF_2] + k_{25}[CF_3{\cdot}CF{:}CF_2][C_2F_4] \quad . \quad . \quad . \quad (27)$$

Whence $$2k_{25}[C_2F_4][CF_3{\cdot}CF{:}CF_2] = k_{24}[CF_3{\cdot}CF{:}CF_2][CF_2] \quad . \quad . \quad . \quad . \quad (28)$$

If, in addition, it is assumed that the molecule–molecule reaction (25) is much slower than the molecule–radical reaction (5), *i.e.*,

$$k_{25}[C_2F_4][CF_3{\cdot}CF{:}CF_2] \ll k_5[C_2F_4][CF_2] \quad . \quad . \quad . \quad . \quad . \quad (29)$$

then $$k_6[CF_3{\cdot}CF{:}CF_2] = k_5[C_2F_4][CF_2] \quad . \quad . \quad . \quad . \quad . \quad . \quad (30)$$

From equations (28) and (30) $$[CF_2]^2 = [CF_3{\cdot}CF{:}CF_2]2k_6k_{25}/k_5k_{24} \quad . \quad . \quad . \quad . \quad (31)$$

It can further be shown that

$$-\mathrm{d}[CF_3{\cdot}CF{:}CF_2]/\mathrm{d}t = 1{\cdot}5[CF_3{\cdot}CF{:}CF_2]^{\frac{1}{2}}\sqrt{(2k_6k_{24}k_{25}/k_5)} \quad . \quad . \quad . \quad (32)$$

The assumption in equation (29) implies that equilibrium between reactions (5) and (6) is almost established before the other reactions have taken place to any noticeable extent. If we predict also that k_{25} is markedly less than k_{24} the apparent induction period can be explained. At first C_2F_4 and CF_2 are formed in equal amounts and are lost in equal amounts by reaction (5) but CF_2 is also lost by reaction (24) whilst little C_2F_4 is lost by reaction (25). At this stage the effective reaction is

$$2CF_3{\cdot}CF{:}CF_2 = C_2F_4 + (CF_3)_2C{:}CF_2 \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (33)$$

and there is no change in volume. Reaction (25) becomes increasingly significant as the C_2F_4 accumulates, until the steady state to which equation (32) refers is established.

Integration of eqn. 32 leads to

$$1/\sqrt{([CF_3{\cdot}CF{:}CF_2])} = (3t/4)\sqrt{(2k_6k_{24}k_{25}/k_5)} + \text{Constant} \quad . \quad . \quad . \quad (34)$$

Values of $\sqrt{(k_6k_{24}k_{25}/k_5)}$ for the various pyrolysis series, obtained from application of eqn. (34) are given in Table 2.

TABLE 2.

Temperature	600°	625°	650°	675°
$10^5\sqrt{(k_6k_{24}k_{25}/k_5)}$ (l.$^{\frac{1}{2}}$ mole$^{-\frac{1}{2}}$ sec.$^{-1}$)	159	447	869	2100

From these values an Arrhenius equation was derived,

$$\sqrt{(k_6k_{24}k_{25}/k_5)} = 3{\cdot}4 \times 10^{10} \exp(-53{,}500/\boldsymbol{R}T) \text{ l.}^{\frac{1}{2}} \text{ mole}^{-\frac{1}{2}} \text{ sec.}^{-1} \quad . \quad (35)$$

Since reactions (5) and (24) are very similar, each involving the addition of a difluoromethylene radical to a simple perfluoro-olefin, we can assume them to have similar values for activation energy and frequency factor, whence

$$E_6 + E_{25} = 107 \text{ kcal./mole} \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (36)$$

$$\sqrt{(A_6A_{25})} = 3{\cdot}4 \times 10^{10} \text{ l.}^{\frac{1}{2}} \text{ mole}^{-\frac{1}{2}} \text{ sec.}^{-1} \quad . \quad . \quad . \quad . \quad . \quad . \quad (37)$$

It is instructive to compare reaction (25) with reaction (1). It can be calculated that at 400°

$$\text{Rate (1)} = 0{\cdot}5[C_2F_4]^2 \text{ mole l.}^{-1} \text{ sec.}^{-1} \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (38)$$

An equimolecular mixture of tetrafluoroethylene and perfluoropropene was pyrolysed at 400° in order to permit reactions (1) and (25) to compete. No perfluoro*iso*butene was detectable by infrared methods, so reaction (1) must have been at least 100 times faster than reaction (25), *i.e.*,

$$k_{25} \leqslant 5 \times 10^{-3} \text{ l. mole}^{-1} \text{ sec.}^{-1} \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (39)$$

If, on the basis of structural similarity, we assign similar frequency factors to reactions (1) and (25), then

$$A_{25} = 10^8 \text{ l. mole}^{-1} \text{ sec.}^{-1} \quad E_{25} \geqslant 32 \text{ kcal./mole} \quad . \quad . \quad . \quad (40)$$

$$A_6 = 10^{13} \text{ sec.}^{-1} \quad E_6 \leqslant 75 \text{ kcal./mole} \quad . \quad . \quad . \quad (41)$$

The activation energies in reactions (2), (4), and (6) are similar, probably because they all involve the breaking of a C–C single bond as the first step. If this is the case, then we should expect these activation energies to exceed the value of D(C–C) for fluorocarbons. This must be taken as evidence favouring Rabinovitch and Reed's value of D(C–C) = 62

kcal.[10] and against Dibeler, Reese, and Mohler's value of 124 kcal.[11] The unusually high frequency factors in (2) and (4) are a feature of ring-opening reactions.

The small material losses and the dust obtained may be ascribed to polymerisation. Atkinson [9] has shown that difluoromethylene can initiate the gas-phase polymerisation of tetrafluoroethylene. Atkinson and Trenwith [2] and Gray and Pritchard [4] reported that the attack of the tetrafluoroethylene pyrolysis system on silica occurs at 550° and above. It is concluded that the attack is probably by the difluoromethylene radical which is then present.

The Disproportionation of Perfluoroisobutene producing Perfluoroethane.—The reaction scheme to be suggested must explain the first-order kinetics, the production of one molecule of perfluoroethane per molecule of reactant destroyed, and the production of conjugated high-molecular weight fluorocarbons. Since perfluoroethane is the major product it is assumed that trifluoromethyl is the most likely intermediate. The following scheme is suggested:

$$(CF_3)_2C{:}CF_2 \longrightarrow CF_3 + CF_3{\cdot}CF{:}CF \quad . \quad . \quad . \quad . \quad . \quad (42)$$

$$CF_3 + (CF_3)_2C{:}CF_2 \longrightarrow CF_3{\cdot}CF_3 + CF_3{\cdot}CF{:}CF \quad . \quad . \quad . \quad . \quad (43)$$

$$CF_3{\cdot}[CF{:}CF]_n + CF_3{\cdot}[CF{:}CF]_m \longrightarrow CF_3{\cdot}[CF{:}CF]_{n+m} + CF_3 \quad . \quad . \quad . \quad (44)$$

$$CF_3{\cdot}[CF{:}CF]_p + CF_3{\cdot}[CF{:}CF]_q \longrightarrow CF_3{\cdot}[CF{:}CF]_{p+q}{\cdot}CF_3 \quad . \quad . \quad . \quad . \quad (45)$$

If M represents $CF_3{\cdot}[CF{:}CF]_r$, where r is any positive integer, and if it is assumed that in the stationary state the concentrations of the intermediates CF_3 and M are constant, then

$$k_{24}[(CF_3)_2C{:}CF_2] + k_{44}[M]^2 = k_{43}[CF_3][(CF_3)_2C{:}CF_2] \quad . \quad . \quad . \quad . \quad (46)$$

$$k_{42}[(CF_3)_2C{:}CF_2] + k_{43}[CF_3][(CF_3)_2C{:}CF_2] = k_{44}[M]^2 + k_{45}[M]^2 \quad . \quad . \quad . \quad (47)$$

whence

$$2k_{42}[(CF_3)_2C{:}CF_2] = k_{45}[M]^2 \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (48)$$

Assuming that the reaction chain length is long, we can show that,

$$-d[(CF_3)_2C{:}CF_2]/dt = 2(k_{42}k_{44}/k_{45})[(CF_3)_2C{:}CF_2] \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (49)$$

Using the integrated form of this equation we obtained the following values of $2k_{42}k_{44}/k_{45}$: at 700°, 37 sec.$^{-1}$; at 725°, 104 sec.$^{-1}$; at 750°, 307 sec.$^{-1}$. The ratio can be expressed as $1{\cdot}1 \times 10^{14} \exp(-82{,}700/RT)$ sec.$^{-1}$. This means that the activation energy for the initial split of perfluoro*iso*butene is not greater than 83 kcal. A similar conclusion is reached when some alternative reaction mechanisms are considered.

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Chemistry Department, Imperial College of Science and Technology,
London, S.W.7. [*Received, December 13th*, 1956.]

[10] Rabinovitch and Reed, *J. Chem. Phys.*, 1954, **22**, 2092.
[11] Dibeler, Reese, and Mohler, *J. Chem. Phys.*, 1952, **20**, 761.

402. *The Activation of Carbon–Carbon Double Bonds by Cationic Catalysts. Part IV.*[1] *The Iodine-catalysed Dimerisation of* 1 : 1-*Diphenylethylene.*

By Alwyn G. Evans, Peter M. S. Jones, and J. H. Thomas.

The kinetics of the reversible iodine-catalysed dimerisation of 1 : 1-diphenylethylene in 2-nitropropane to its dimer 1 : 1 : 3 : 3-tetraphenylbut-1-ene have been studied dilatometrically. The effect of the reagent concentrations on the reaction rates, and the forward and reverse activation energies have been measured. A mechanism for the dimerisation is proposed.

At low iodine concentrations the reaction does not reach true equilibrium, indicating that the catalyst is converted into some unreactive form, which, it is suggested, may be a π-complex between the iodine and the olefin.

In Parts I and II of this series [1] we investigated dilatometrically the reversible dimerisations, catalysed by trichloroacetic acid, of several 1 : 1-diarylethylenes (M) to the corresponding dimers (1 : 1 : 3 : 3-tetra-arylbut-1-enes) (D), and concluded that the reaction mechanism was :

$$x\mathrm{AH} + \mathrm{M} \underset{b}{\overset{a}{\rightleftharpoons}} (\mathrm{HM^+A^-})_{\mathrm{solv.}} \quad \text{(i)}$$

$$(\mathrm{HM^+A^-})_{\mathrm{solv.}} + \mathrm{M} \underset{b}{\overset{a}{\rightleftharpoons}} (\mathrm{HD^+A^-})_{\mathrm{solv.}} \quad \text{(ii)}$$

$$(\mathrm{HD^+A^-})_{\mathrm{solv.}} \underset{b}{\overset{a}{\rightleftharpoons}} \mathrm{D} + x\mathrm{AH} \quad \text{(iii)}$$

where, in benzene solution, x is 3, and the solvation shell of the carbonium ion intermediates includes two molecules of dimeric trichloroacetic acid (AH).

The equilibrium (i) was confirmed by spectrophotometry (Parts II and III [1]) for the 1 : 1-di-*p*-methoxyphenylethylene–trichloroacetic acid–benzene system, and the carbonium ion was shown to be the reactive intermediate in the dimerisation.

It has been shown by Hildebrand [2] that iodine changes 1 : 1-diphenylethylene to a solid dimer, which with iodine in warm acetic acid gives back some of the monomeric olefin. The solid dimer was later shown to be 1 : 1 : 3 : 3-tetraphenylbut-1-ene.[3]

In this paper we present the results of our dilatometric studies on the iodine-catalysed dimerisation of 1 : 1-diphenylethylene in 2-nitropropane.

Experimental

Materials.—1 : 1-Diphenylethylene and benzene were purified as outlined in Part I,[1a] and 1-methyl-1 : 3 : 3-triphenylindane as in Part III.[1c]

1 : 1 : 3 : 3-Tetraphenylbut-1-ene was prepared either as in Part I or by treating a benzene solution of 1 : 1-diphenylethylene with iodine. In the latter method the solution was shaken after 7 days with excess of sodium thiosulphate solution to remove the iodine, and the organic layer washed with water. The benzene was distilled off, and the resultant solid washed with methanol. The solid material from both preparations was recrystallised from light petroleum (b. p. 60—80°) and fused under a high vacuum. The product was recrystallised twice from dry light petroleum (b. p. 60—80°) and had m. p. 112—113°. This showed it to be 1 : 1 : 3 : 3-tetraphenylbut-1-ene.[3]

Iodine was "AnalaR" material. It was purified either by sublimation under a high vacuum, or by recrystallisation from dry benzene. The method of purification did not affect the results.

[1] (*a*) Part I, Evans, N. Jones, and Thomas, *J.*, 1955, 1824; (*b*) Part II, Evans, N. Jones, P. M. S. Jones, and Thomas, *J.*, 1956, 2757; (*c*) Part III, Evans, P. M. S. Jones, and Thomas, *J.*, 1957, 104.
[2] Hildebrand, Diss., Strassburg, 1909.
[3] Lebedev, Andreewsky, and Matynsekina, *Ber.*, 1923, **56**, 2350.

2-Nitropropane (from Messrs. Light) was kept over phosphoric oxide for 24 hr., then distilled off under reduced pressure and fractionated twice up a 40 cm. Vigreux column, the middle fraction, b. p. 120°, being retained (lit.,[4] b. p. 120°).

The nitrobenzene, *m*-nitrotoluene, ethylene dichloride, and *n*-hexane were all purified in the same way. They were kept over phosphoric oxide for 24 hr., then fractionated. The middle fraction was retained and refractionated. In the case of ethylene dichloride a further fractionation off anhydrous potassium carbonate was used to remove any hydrogen chloride. The middle fraction was retained in each case, the b. p.s being: nitrobenzene, 210—211° (lit.,[5] b. p. 210·8°); *m*-nitrotoluene, 230—232° (lit.,[6] b. p. 232·6°); ethylene dichloride, 83—84° (lit.,[7] b. p. 83·5°); *n*-hexane, 68—69° (lit.,[5] b. p. 68·8°).

Procedure.—The iodine was weighed directly and made up to a known concentration in the solvent. A suitable known volume was pipetted into a 100 ml. flask containing a weighed amount of monomer or dimer in solution. The mixture was made to the mark with the solvent, and the solution shaken.

The dilatometers were filled and the volumes of the solutions followed with time in thermostat baths at 54·6°, 45·9°, and 33·8°, as outlined in Part I.

The solutions were analysed when all the volume change had ceased, by shaking the contents of the dilatometers with a known excess of sodium thiosulphate solution. The iodine in the solution was then estimated by back-titration with iodine solution. The organic layer was separated off, washed with water, and evaporated to dryness under a high vacuum. The residual oily solid was washed with absolute methanol to remove residual monomer (the dimer is not very soluble in this medium). The product thus obtained was weighed, and its m. p. recorded.

n-Hexane solutions containing known concentrations of 1 : 1 : 3 : 3-tetraphenylbut-1-ene, 1-methyl-1 : 3 : 3-triphenylindane, reaction product, and mixtures of both dimers were examined spectrophotometrically with a Unicam SP500 spectrophotometer and 1 cm. silica optical cells.

Results

Iodine-catalysed Dimerisation in 2-Nitropropane.—(a) *Nature of reaction products.* Solutions of iodine, 1 : 1-diphenylethylene, 1 : 1 : 3 : 3-tetraphenylbut-1-ene, or 1-methyl-1 : 3 : 3-triphenylindane, separately in 2-nitropropane, showed no volume change at 54·6° during 9 months. The unchanged materials were recovered completely after this time.

Density measurements on solutions of 1 : 1-diphenylethylene and 1 : 1 : 3 : 3-tetraphenylbut-1-ene separately in 2-nitropropane (as in Part I) show that the volume changes accompanying the complete conversion of 1 mole of monomer into 0·5 mole of but-1-ene in 1 l. of solution are 12·40 ml. at 33·8°, 12·41 ml. at 45·9°, and 12·75 ml. at 54·6°.

Mixed solutions of 1 : 1-diphenylethylene and iodine in 2-nitropropane give a volume decrease (Fig. 1, curve *A*), while those containing 1 : 1 : 3 : 3-tetraphenylbut-1-ene and iodine in 2-nitropropane give a volume increase (Fig. 1, curve *B*). Both sets of solutions reach a steady unchanging volume after some time, and analysis of such solutions gives a 100 ± 3% recovery of the iodine, together with weight of solid butene equal to within 5% of that expected from the volume change.

The crude dimer isolated from the solutions had, when washed with methanol, a m. p. within the range 106—112°; this rose after one recrystallisation from light petroleum (b. p. 60—80°) to 112—113°, showing the product to be 1 : 1 : 3 : 3-tetraphenylbut-1-ene.[3]

In view of the low m. p. of some of the samples of dimer isolated it was thought possible that traces of 3-methyl-1 : 3 : 3-triphenylindane might be formed. Solutions of the indane and butene in *n*-hexane had absorption peaks at 264 and 255 mμ respectively, and both obeyed Beer's law (ε_{264} for 1-methyl-1 : 3 : 3-triphenylindane is $1{\cdot}30 \times 10^3$; ε_{255} for 1 : 1 : 3 : 3-tetraphenylbut-1-ene is $1{\cdot}14 \times 10^4$). No indane could be detected from the absorption spectra of solutions of the crude product in *n*-hexane. (This absorption method would show the presence of indane if more than 3% were present.) A dilatometric run using a 2-nitropropane

[4] "International Critical Tables," McGraw Hill Book Co., Inc., New York, 1929, Vol. III, p. 180.
[5] Timmermans, "Physical Chemical Constants of Pure Organic Liquids," Elsevier, Amsterdam, 1950.
[6] De Beule, *Bull. Soc. chim. belges*, 1933, **55**, 3633.
[7] Coulson, Hales, and Herington, *Trans. Faraday Soc.*, 1948, **44**, 636.

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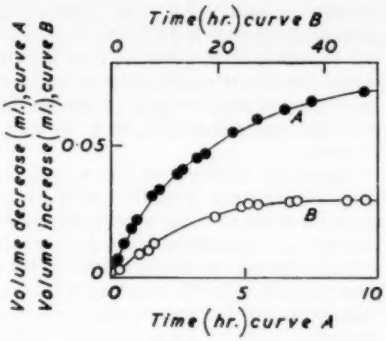
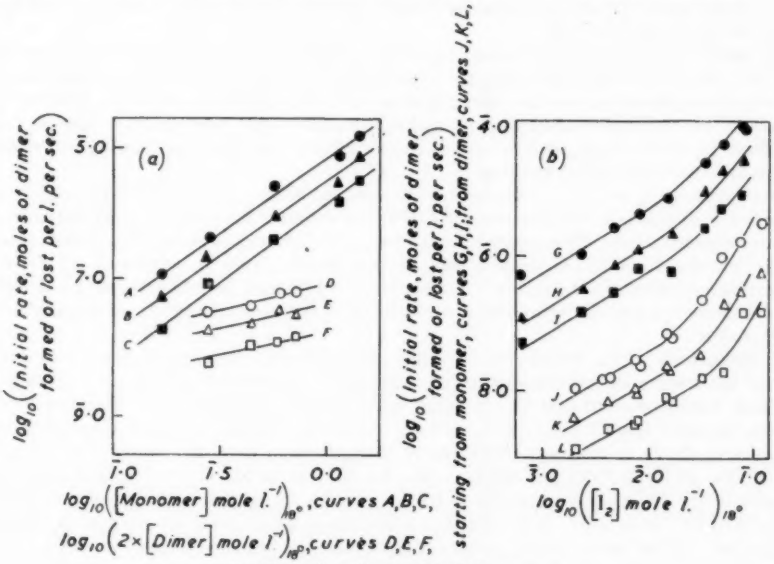


FIG. 1. *Volume–time curves for the iodine-catalysed dimerisation in 2-nitropropane.*

A, Dimerisation reaction: initial 1 : 1-*diphenylethylene concn.* 0·550 *mole* $l.^{-1}$; *initial iodine concn.* $7·15 \times 10^{-2}$ *mole* $l.^{-1}$; *initial vol. of solution* 29·9 *ml.; temp.* 33·8°.

B, Reverse reaction: initial 1 : 1 : 3 : 3-*tetraphenylbut*-1-*ene concn.* 0·136 *mole* $l.^{-1}$; *initial iodine concn.* $7·1 \times 10^{-2}$ *mole* $l.^{-1}$; *initial vol. of solution* 26·8 *ml.; temp.* 54·6°.

FIG. 2. *Dependence of initial rate on concentrations of monomer, dimer, and iodine.*



(*a*) *Variation of rate with olefin concn.*

Curve	Temp.	Initial I_2 concn. (10^{-2} mole $l.^{-1}$)	Slope
A	54·6°	1·50	2·0 ± 0·2
B	45·9	1·52	2·0 ± 0·2
C	33·8	1·54	2·0 ± 0·2
D	54·6	1·50	0·9 ± 0·2
E	45·9	1·52	0·95 ± 0·2
F	33·8	1·54	0·9 ± 0·2

(Curve *B* has been lowered vertically by 0·2, and curve *C* by 0·4.)

(*b*) *Variation of rate with iodine concn.*

Curve	Temp.	Initial monomer concn. (mole $l.^{-1}$)	Curve	Temp.	Initial dimer concn. (mole $l.^{-1}$)
G	54·6°	0·540	*J*	54·6°	0·285
H	45·9	0·545	*K*	45·9	0·288
I	33·8	0·550	*L*	33·8	0·291

(Curve *G* has been raised vertically by 0·5, curve *H* raised by 0·2, curve *K* lowered vertically by 0·3, and curve *L* lowered by 0·2.)

solution of iodine ($5{\cdot}5 \times 10^{-2}$ mole $l.^{-1}$), and saturated with respect to 1-methyl-1 : 3 : 3-triphenylindane ($5{\cdot}8 \times 10^{-2}$ mole $l.^{-1}$), gave no volume change at 54·6° during 5 months, at the end of which both materials were completely recovered. Any formation of indane, under the conditions of our experiments, would therefore be irreversible, and all the olefin would in time be converted into indane. Since the dimer even after several months at equilibrium always contained more than 97% of 1 : 1 : 3 : 3-tetraphenylbut-1-ene, no indane can be formed in the reaction.

Since the amounts of dimer recovered from the reaction mixtures agree closely with the amounts expected from the volume change, we may take these volume changes as giving an accurate measure of the extent of conversion of monomer into dimer or *vice versa*. Any volume changes accompanying olefin–iodine interaction must therefore be small compared with the volume changes on dimerisation. This is to be expected since the olefin was always in excess over the iodine in the reacting solutions; the ratio [1 : 1-diphenylethylene] : [iodine] varying from 6 to 10^3 for the forward reaction in 2-nitropropane, and the ratio [1 : 1 : 3 : 3-tetraphenylbut-1-ene] : [iodine] varying from 2·8 to 10^2 for the reverse reactions.

(b) *Initial rates of reaction.* The volume–time curves (of type shown in Fig. 1) were analysed by the method of initial slopes as in Part I, and the initial rates converted into moles of dimer formed or lost per l. per sec. by using the volume changes for complete reaction found from the density measurements (above).

The initial rate of the reaction and the total volume change were not affected by light, or by the surface area of the dilatometer. This was shown by comparing three solutions of the same initial monomer and iodine concentrations in 2-nitropropane, one in an ordinary dilatometer bulb, one in a bulb surrounded by tinfoil to exclude light, and one in a bulb packed with glass chips to give a large surface area. Degassing the solutions and sealing off under high vacuum had no effect on the reaction.

(c) *Dependence of the initial rate on the olefin concentration.* The initial rates were measured for a series of solutions having the same initial iodine concentration and varying initial monomer or dimer concentration. Plots were made of $\log_{10}$ (initial rate) against $\log_{10}$ [initial monomer] (Fig. 2*a*, curves *A*, *B*, *C*), or against $\log_{10}$ [initial dimer] (Fig. 2*a*, curves *D*, *E*, *F*), both at constant initial iodine concentration. These plots were straight lines the slopes of which give the orders in monomer and dimer as 2·0 ± 0·2 and 0·9 ± 0·2 respectively, at all three thermostat temperatures.

(d) *Dependence of the initial rate on iodine concentration.* The initial rates were measured similarly for a series of solutions of constant initial 1 : 1-diphenylethylene or 1 : 1 : 3 : 3-tetraphenylbut-1-ene concentration and varying initial iodine concentration. Plots were made of $\log_{10}$ (initial rate) against $\log_{10}$ [initial iodine] at constant initial monomer concentration (Fig. 2*b*, curves *G*, *H*, *I*) or constant initial dimer concentration (Fig. 2*b*, curves *J*, *K*, *L*). These were curves, showing that the order of the reaction in terms of total iodine concentration increases (0·8 to 2·1) as the iodine concentration increases over the range of concentrations used (6×10^{-4} to 10^{-1} mol. $l.^{-1}$). It is seen that the order in iodine does not vary with temperature and that for a given iodine concentration it is practically the same for both the forward and the reverse reaction. The parallelism of the two sets of curves is excellent for the two lower temperatures.

(e) *Rate constants.* In view of the changing iodine order the rate constants will be defined by equations of the type:

$$\text{Initial forward rate} = k_f[\mathrm{M}]^2[\mathrm{I}_2]_t^x$$

$$\text{Initial reverse rate} = k_r[\mathrm{D}][\mathrm{I}_2]_t^x$$

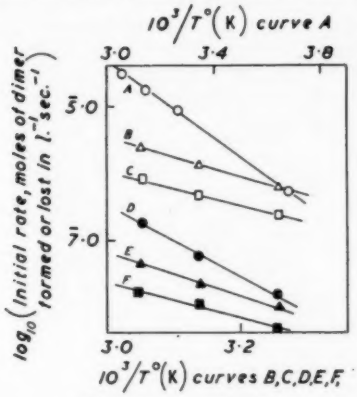
where forward rate refers to the dimerisation reaction, [M] is the monomer concentration, [D] the dimer concentration, $[\mathrm{I}_2]_t$ is the total iodine concentration, and k_f and k_r are the forward and reverse rate constants respectively, and x is the iodine order appropriate for the particular iodine concentration used. (As the two sets of curves in Fig. 2*b* are parallel, x will be the same for both forward and reverse reaction at any given iodine concentration.) We give values of of k_f and k_r for systems in which x is 1 ± 0·15 (*i.e.*, where $[\mathrm{I}_2]_t$ is between 2×10^{-3} and 2×10^{-2} mole $l.^{-1}$) in Table 1.

(f) *Forward and reverse activation energies.* These have been found by measuring the initial rates of the forward and the reverse reaction at 33·8°, 45·9°, and 54·6°, for several series of solutions having constant initial iodine and olefin concentrations at room temperature.

The activation energies are then found from plots of $\log_{10}$ (initial rate) against $1/T°$ K, as shown in Fig. 3, after correcting for the small change in reagent concentrations due to thermal expansion, as in Part I.

Over the range of unit iodine order the activation energies are constant and have the values $E_f = 12{\cdot}3 \pm 0{\cdot}7$ kcal. mole^{-1} for the forward reaction, and $E_r = 19{\cdot}4 \pm 0{\cdot}8$ kcal. mole^{-1} for the reverse reaction. Both are independent of the olefin and iodine concentrations.

FIG. 3. *Activation energies for the forward and reverse reactions.*



All concns. in mole l.$^{-1}$.

Curve	[Initial monomer]$_{18°}$	[Total iodine]$_{18°}$	Iodine order x	E_f (kcal. mole^{-1})
A	0·565	0·073	1·9	14·5
B	0·565	0·0157	1·1	12·6
C	0·565	0·00465	1·0	12·3
	[Initial dimer]$_{18°}$			E_r (kcal. mole^{-1})
D	0·142	0·113	2·1	24·3
E	0·221	0·0157	1·1	19·3
F	0·286	0·00403	0·9	19·2

(Curve *D* has been lowered by 1·0.)

Above this range of iodine concentration the activation energies increase with increasing iodine concentration, rising to 14·5 kcal. mole^{-1} for the forward runs at $7{\cdot}3 \times 10^{-2}$ mole l.$^{-1}$ of iodine, and 24·3 kcal. mole^{-1} for the reverse runs at a similar iodine concentration. It was not possible to use higher concentrations of iodine because these solutions were almost saturated.

(g) *Entropies of activation.* The entropies of activation $\Delta S_f^{\ddagger}$ and $\Delta S_r^{\ddagger}$ for the forward and the reverse reaction respectively have been found (as in Part II) for the range of unit iodine order and constant activation energy. The values thus obtained are given in Table 1.

TABLE 1. *The rate constants, activation energies, and entropies of activation, for the iodine-catalysed dimerisation of* 1 : 1*-diphenylethylene.**

Temp.	Rate constant	Activation energy (kcal. mole^{-1})	Entropy of activation (cal. mole^{-1} deg.$^{-1}$)
Forward reaction	k_f (mole^{-2} l.^{2} sec.$^{-1}$)	E_f	$-\Delta S_f^{\ddagger}$
33·8°	$2{\cdot}3 \times 10^{-4}$	12·3 ± 0·7	38·1
45·9	$3{\cdot}2 \times 10^{-4}$		38·4
54·6	$4{\cdot}6 \times 10^{-4}$		39·0
Reverse reaction	k_r (mole^{-1} l. sec.$^{-1}$)	E_r	$-\Delta S_r^{\ddagger}$
33·8°	$2{\cdot}4 \times 10^{-6}$	19·4 ± 0·8	23·8
45·9	$6{\cdot}9 \times 10^{-6}$		24·0
54·6	$1{\cdot}24 \times 10^{-5}$		24·3

* These figures only apply to solutions having an iodine concentration between 2×10^{-3} and 2×10^{-2} mole l.$^{-1}$, where the iodine order is unity (see text). The rates and entropies refer to the 1 mole l.$^{-1}$ standard state.

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(h) *Volume changes during reaction.* Since the iodine orders for the forward and the reverse reaction are the same, the volume changes occurring from the initial to the equilibrium position of the system V_e, should be a function of the olefin concentration only, as in the dimerisations catalysed by trichloroacetic acid (Parts I and II). This is however found not to be the case; for the same weight of initial olefin the volume change in these reactions, V^*, is less at low iodine concentration than at high iodine concentration. Plots of V^*, for a given weight of initial olefin, against iodine concentration are curves of the type shown in Fig. 4.

If this dependence on the initial iodine concentration were due to differing iodine orders for the forward and reverse reactions, then the values of V^* starting from equal weights of monomer and dimer should be complementary, and their sum at any iodine concentration should be constant. This is not the case, however. For systems of low iodine concentration the same final monomer–dimer mixture is not obtained from two solutions of equal iodine concentration, one containing a given initial weight of monomer and the other the same initial weight of dimer.

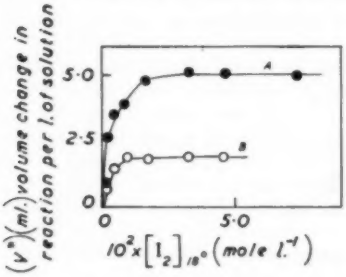
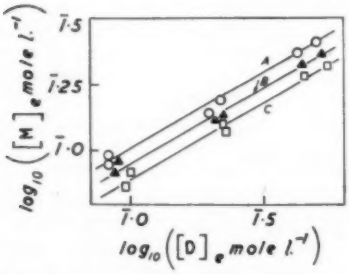
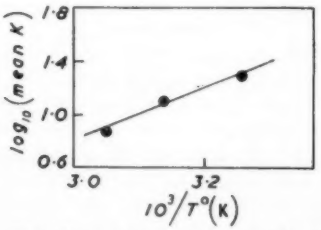


FIG. 4. *Dependence of V^* on iodine concn.*
A, Constant initial 1 : 1-*diphenylethylene concn.* 0·540 *mole* $l.^{-1}$ *at* 54·6°.
B, Constant initial 1 : 1 : 3 : 3-*tetraphenylbut*-1-*ene concn.* 0·285 *mole* $l.^{-1}$ *at* 54·6°.

FIG. 5. *Equilibrium concentrations of monomer and dimer, and the temperature-dependence of the equilibrium constant.*



(a) *Plot of* $\log_{10}[M]_e$ *against* $\log_{10}[D]_e$.
A, 54·6°, *slope* 0·5 ± 0·1.
B, 45·9°, *slope* 0·5 ± 0·1.
D, 33·8°, *slope* 0·5 ± 0·1.



(b) *Plot of* $\log_{10}$ (*mean K*) *against* $1/T$ (°K).

The monomer–dimer mixture which is obtained indicates that the reaction has stopped before complete equilibrium has been reached.

Since the sole product isolated from the reaction mixtures is the dimer, 1 : 1 : 3 : 3-tetraphenylbut-1-ene, and its concentration always agrees to within 5% with the observed volume change, the only possible explanation is that the iodine catalyst is converted in some way into an unreactive species, the reaction thus stopping short of equilibrium.

When the iodine concentration is sufficiently high, V^* becomes independent of it, as seen in Fig. 4 (where the iodine concentration is >5% of initial olefin). The sum of the forward and the reverse volume changes for equal initial weights of monomer and dimer is then constant at all three temperatures. If a true equilibrium is reached at these high iodine concentrations, these sums should be equal to the volume change accompanying complete conversion of monomer into dimer. The volume changes accompanying the complete conversion of 1·0 mole of monomer into 0·5 mole of but-1-ene in 1 l. of solution would, from these sums, be 12·5 ml. at 33·8°, 12·3 ml. at 45·9°, and 12·7 ml. at 54·6°. These values agree to within 2% with

those found above from density measurements, thus confirming that a true equilibrium is attained at high iodine concentrations. (*i.e.*, $V^* = V_e$), and that the position of equilibrium is not then dependent on the iodine concentration.

(i) *Equilibrium constants.* The volume changes at high iodine concentration (when $V^* = V_e$) give a value for the concentration of dimer or monomer formed in the reaction when it reaches a true equilibrium. The concentrations of unchanged monomer or dimer can be calculated from their initial concentrations at the bath temperatures.

Thus for any solution the equilibrium concentrations of monomer $[M]_e$ and dimer $[D]_e$ can be obtained. A plot of $\log_{10}[M]_e$ against $\log_{10}[D]_e$ is given for each bath temperature in

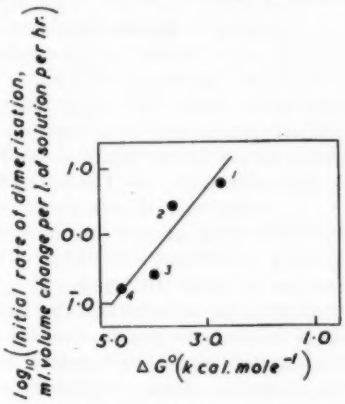


FIG. 6. *Variation of initial rate with solvent.*

Plot of $\log_{10}$ *(initial rate) at 54·6° for initial iodine concn. 0·076 mole l.*$^{-1}$ *and initial 1 : 1-diphenylethylene concn. 0·540 mole l.*$^{-1}$*, against the free-energy change,* $\Delta G°$*, for the ionisation of tri-*p*-tolylmethyl chloride.*

The numbers on the points signify the solvents: 1, $PhNO_2$; 2, Pr^iNO_2; 3, *m*-$C_6H_4Me{\cdot}NO_2$; 4, $(CH_2Cl)_2$.

Fig. 5*a*. These plots are all straight lines of slope $0·5 \pm 0·1$. Thus as in Part II the equilibrium constant, K, for the dimerisation is given by :

$$K = [D]_e/[M]_e^2$$

The mean values of the equilibrium constants found in this way for solutions reaching true equilibrium are given in Table 2.

TABLE 2. *Thermodynamic constants for the dimerisation of* 1 : 1*-diphenylethylene.*

Catalyst	Solvent	K (°c) (mole^{-1} l.)	$-\Delta G°$ (kcal. mole^{-1})	$-\Delta H°$ (kcal. mole^{-1})	$-\Delta S°$ (cal. mole^{-1} deg.$^{-1}$)
I_2	Pr^iNO_2	18·5 (33·8°)	1·79 ± 0·05	9·7 ± 1·0	25·7 ± 5
		13·4 (45·9°)			
		7·0 (54·6°)			
$CCl_3{\cdot}CO_2H$ *	C_6H_6	15·9 (33·8°)	1·59 ± 0·05	10·0 ± 0·5	27·1 ± 2
$CCl_3{\cdot}CO_2H$ *	$EtNO_2$	13·4 (34·2°)	1·59 ± 0·05	9·7 ± 0·5	25·7 ± 2

* Taken from Parts I and II of this series.[1]

(j) *Exothermicity of the dimerisation.* A plot of $\log_{10}$ (mean K) against $1/T°K$ was made, as shown in Fig. 5*b*, and the exothermicity ($-\Delta H°$) found from its slope to be $9·7 \pm 1·0$ kcal. mole^{-1} (see Table 2).

Effect of Solvent on the Dimerisation Rate.—A series of dilatometric runs was carried out at 54·6° with the solvents nitrobenzene, 2-nitropropane, *m*-nitrotoluene, and ethylene dichloride. The initial iodine (0·076 mole l.$^{-1}$) and initial 1 : 1-diphenylethylene (0·540 mole l.$^{-1}$) concentrations were identical in each solvent.

The initial rates were measured as previously outlined. Each of the solvents gave normal volume–time curves (volume decreasing with time) of the type shown in Fig. 1.

The contents of the dilatometers were analysed when the volume change ceased, and the product isolated in each case was shown by its m. p. (112—113°) to be 1 : 1 : 3 : 3-tetraphenylbut-1-ene.

A plot of $\log_{10}$ (initial rate of volume decrease per l. of solution) against the free energy change $\Delta G°$ for the ionisation of tri-*p*-tolylmethyl chloride in the same solvents [a] according to

[a] Evans, Price, and Thomas, *Trans. Faraday Soc.*, (*a*) 1955, **51**, 481; (*b*) 1954, **50**, 470, 568; (*c*) 1956, **52**, 332.

the equation, $RCl \longrightarrow R^+Cl^-$ (Fig. 6), shows a roughly linear correlation. It must be stressed that this correlation is purely qualitative, since (i) the reagent orders may differ from solvent to solvent, and (ii) the volume changes accompanying dimerisation may differ slightly from solvent to solvent. The latter effect will not be large, as is shown by the close similarity of the volume changes accompanying complete dimerisation of 1 : 1-diphenylethylene in benzene,[1a] nitroethane,[1b] and nitropropane (this paper). The initial rates measured in rate of volume change per l. of solution will therefore give a reasonable measure of the initial rate of formation of dimer.

Discussion

The Reaction Mechanism.—Any mechanism must account for the following observations. (*a*) The sole product of the iodine-catalysed dimerisation of 1 : 1-diphenylethylene is 1 : 1 : 3 : 3-tetraphenylbut-1-ene. (*b*) The dimerisation is reversible, not affected by light or by the surface of the reaction vessel. (*c*) The iodine titratable with sodium thiosulphate at the end of the reaction is equal, within experimental error (±3%), to the total initial iodine concentration. (*d*) The initial rate of the forward reaction is second order in total monomer. (*e*) The initial rate of the reverse reaction is first order in total dimer. (*f*) The initial rate of both the forward and the reverse reaction are of the same order with respect to total iodine; the value of this order is $1 \pm 0{\cdot}1$ for iodine concentrations between about 2×10^{-3} and 2×10^{-2} mole $l.^{-1}$, and rises rapidly to a value of 2·0 at iodine concentrations of about 10^{-1} mole $l.^{-1}$ (It is not experimentally possible to extend the iodine concentration further than the 200-fold range we have used.) (*g*) Over the experimental range studied, the monomer–dimer equilibrium is fully established for iodine concentrations greater than about 10^{-2} mole $l.^{-1}$. At iodine concentrations below this value, however, the monomer–dimer equilibrium is not established completely. This lack of equilibrium becomes more marked the lower the iodine concentration, although the total iodine can still be completely estimated by sodium thiosulphate.

These facts can be interpreted by the following reaction system:

$$C_s + M \underset{b}{\overset{a}{\rightleftharpoons}} (CM)_s^* \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (1)$$

$$(CM)_s^* + M \underset{b}{\overset{a}{\rightleftharpoons}} (CD)_s^* \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (2)$$

$$(CD)_s^* \underset{b}{\overset{a}{\rightleftharpoons}} C_s + D \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (3)$$

where M is monomer, D is dimer, C_s is the solvated catalyst, $(CM)_s^*$ and $(CD)_s^*$ are solvated polar intermediates formed by reaction of catalyst with monomer and of catalyst with dimer respectively. These equations will explain the experimental points (*a*), (*b*), (*d*), and (*e*), if we take reaction (2*a*) as rate-determining for the forward reaction, and reaction (2*b*) or (3*b*) as rate-determining for the reverse process. On this basis the following rate equations can be written:

$$\begin{aligned} \text{Rate of forward reaction} &= k_{2a}K_1[M]^2[C_s] \\ \text{Rate of reverse reaction} &= k_{2b}K_3^{-1}[D][C_s] \\ \text{or} &= k_{3b}[D][C_s] \end{aligned}$$

The order of the reaction in total iodine can be interpreted according to reactions (4) and (5), if I_2 and/or I^+I^- and $I^+I_3^-$ can act as the catalyst C.

$$I_2 \rightleftharpoons I^+I^- \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (4)$$

$$I_2 + I_2 \rightleftharpoons I^+I_3^- \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (5)$$

At low iodine concentrations the equilibrium (4) will predominate, and if the catalyst C_s were I_2 and/or I^+I^-, its kinetic effect would be of first order in total iodine. At high

iodine concentrations the species $I^+I_3^-$ will predominate, and if this is acting as catalyst, C_s, its kinetic effect will be of second order in total iodine. This interpretation would necessitate the iodine order's remaining unity for all iodine concentrations lower than those studied, and rising to a maximum of 2 for all iodine concentrations higher than those used. As regards point (*g*), the lack of monomer–dimer equilibrium at low iodine concentrations suggests that iodine is slowly converted into a non-catalytic form, in which, however, it can be completely titrated with sodium thiosulphate. Since solutions of iodine in 2-nitropropane have always the same catalytic activity independent of the length of time they have been made up, it seems clear that the reaction of iodine which leads to its loss of catalytic activity is a reaction between it and the monomer or dimer :

$$C_s + M \rightleftharpoons (CM)_s\dagger \quad . . . . . (6)$$

or

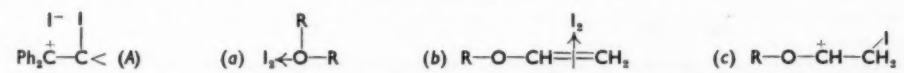
$$C_s + D \rightleftharpoons (CD)_s\dagger \quad . . . . . (7)$$

where the equilibria are well over to the right, and where $(CM)_s\dagger$ and $(CD)_s\dagger$ differ from the intermediates $(CM)_s^*$ and $(CD)_s^*$ of equation (1), (2), and (3) in the fact that they do not react further.

By analogy with the work of the previous Parts, where it was found for the acid-catalysed dimerisation that the active intermediate was the carbonium ion, we postulate that $(CM)_s^*$ and $(CD)_s^*$ are carbonium ions of the type (*A*) where the negative ion may be I^-, as written, or I_3^-, if $I^+I_3^-$ is acting as the catalyst (see reaction 5). Since the catalyst, however, is not a proton donor, this dimerisation differs from that of the acid-catalysed reaction (Parts I and II) in that the formation of the dimer involves migration of a hydrogen atom from one monomer to the other. If the carbonium ion postulated above is the active intermediate, there will also be an accompanying migration in the opposite direction of a covalently bonded iodine atom.

If $(CM)_s^*$ and $(CD)_s^*$ are carbonium ions, it seems plausible that the non-reactive species $(CM)_s\dagger$ and $(CD)_s\dagger$ should be π-complexes. In Part III we give evidence that the π-complex formed between acid and olefin is produced more slowly than is the carbonium ion, but its final equilibrium position lies much further over to the complex side. We therefore suggest that the iodine in solution is slowly converted into a π-complex with the olefin, the iodine acting as an electron-acceptor, and the olefinic double bond as an electron-donor. The possibility that the iodine is deactivated by forming an iodide with the olefin is unlikely (*a*) because the total iodine is titratable at the end of the experiment, and (*b*) because this iodide has never been isolated.

The more iodine in solution, the longer it would take for its concentration to be reduced sufficiently to stop the reaction, and the closer would the forward and the reverse reaction approach their true equilibrium positions. Eley and Richards [9] have studied the iodine-catalysed polymerisation of vinyl ethers and in order to interpret their results postulate three products of interaction between iodine and the vinyl ether :



These authors conclude that the carbonium ion (*c*) is the reactive intermediate in the polymerisation, while the π-complex (*b*) is also present as an unreactive species which has the effect of reducing the concentration of active iodine. The catalytically active iodine is taken to be I^+ produced by the interaction of two molecules of type (*a*).

Rate and Equilibrium Constants.—It can be seen from Tables 1 and 2 that the ratio of the rate constants differs considerably from the overall equilibrium constant for the dimerisation. As will be described in a later paper, we find that there is extensive complex-formation between the iodine and the benzene rings of the monomer and the olefinic dimer,

[9] Eley and Richards, *Trans. Faraday Soc.*, 1949, **45**, 425; Eley and Saunders, *J.*, 1952, 4167.

and we believe that the solvation of the catalyst, C(I_2, and/or I^+I^-, and $I^+I_3^-$) consists mainly of this type of complex-formation. The catalyst for the initial stage of the forward reaction will therefore be different from that for the initial stage of the reverse reaction, and thus the ratio of the initial rate constants k_f/k_r will not be equal to K. These reactive benzene–iodine complexes are similar in type to that postulated by Eley and Richards [see structure (*a*) above].

One of us (P. M. S. J.) thanks the Department of Scientific and Industrial Research for a maintenance allowance.

UNIVERSITY COLLEGE, CARDIFF. [*Received, December 27th,* 1956.]

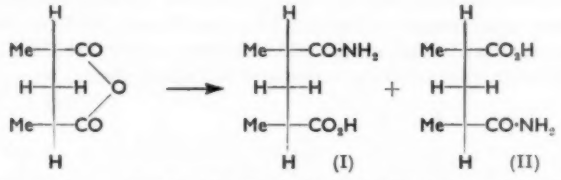
403. *Synthesis of Potential Antibacterial Agents. Part III.* Derivatives of Some αα′-Dialkylglutaric Acids.*

By D. W. S. EVANS and JOHN C. ROBERTS.

A number of substituted glutaramic acids have been synthesised (by treatment of the appropriate anhydrides with ammonia or primary amines), and their antibacterial activities *in vitro* have been determined.

IN this paper we extend the work described in Part I [1] to derivatives of αα′-dimethyl- and αα′-diethyl-glutaric acids. All these derivatives possess, in addition to the acidic group, one of the following potential antibacterial groupings: carbamoyl, *N*-phenyl-, *N*-*p*-chlorophenyl-, *N*-*p*-sulphamoylphenyl-, *N*-2′-pyridyl-, or *N*-2′-thiazolyl-carbamoyl.

The required αα′-dialkylglutaric acids were obtained by hydrolysis and decarboxylation of the corresponding ethyl 1 : 3-dialkylpropane-1 : 1 : 3 : 3-tetracarboxylates. In order to avoid stereochemical complications in the synthesis of the dialkylglutaramic acids (see below) it was necessary to use either the racemic or the *meso*-anhydrides. We therefore chose to work, in the first instance, with the *meso*-anhydrides because they are more readily available. *meso*-αα′-Dimethylglutaric anhydride was prepared directly from the mixture of the concomitantly produced *meso*- and racemic acid by treatment with acetyl chloride.[2] A number of attempts to prepare *meso*-αα′-diethylglutaric anhydride by a direct method from the mixed acids were unsuccessful. Separation of the mixed acids into *meso*- and racemic forms was attempted by partition chromatography on a silica column,[3] but was abortive. We therefore separated the *meso*-acid by fractional crystallisation and converted it into the anhydride, a crystalline solid of low melting point (it had been reported [4] as an oil).



αα′-Dialkylglutaramic or *N*-substituted αα′-dialkylglutaramic acids were then obtained by treatment of the *meso*-anhydrides, in a dry organic solvent, with ammonia or primary amines. It should be emphasised that these derivatives are in the forms of single racemates (*e.g.*, I + II) since the *meso*-anhydride ring may open, with equal facility, in the two

* Part II, *J.*, 1952, 4935.

[1] Roberts and Shaw, *J.*, 1950, 2842.
[2] Auwers and Thorpe, *Annalen*, 1895, **285**, 327.
[3] Cf. Roberts and Selby, *J.*, 1951, 2335.
[4] (*a*) Reformatsky, *J. Russ. Phys. Chem. Soc.*, 1902, **34**, 357; (*b*) cf. Berner and Landmark, *Acta Chem. Scand.*, 1953, **7**, 1347.

possible ways. (Some *N*-substituted derivatives of glutaramic acid itself were also prepared.)

A few of the compounds investigated showed slight antibacterial activity.

Experimental

Starting Materials.—Ethyl propane-1 : 1 : 3 : 3-tetracarboxylate was prepared by Welch's method.[5] One fractionation of the crude material (through an externally heated 15″ column of Fenske helices) gave a colourless oil (62% yield), b. p. 193°/9 mm. (Found : C, 54·2; H, 7·3. Calc. for $C_{15}H_{24}O_8$: C, 54·2; H, 7·3%). An alternative method [6] gave lower and variable yields. Ethyl pentane-2 : 2 : 4 : 4-tetracarboxylate was obtained by methylation of the foregoing ester; [7] two fractionations of the crude material yielded the pure ester (21% yield), b. p. 165°/1·2 mm. (Found : C, 56·4; H, 7·4. Calc. for $C_{17}H_{28}O_8$: C, 56·6; H, 7·8%). By using ethyl iodide, ethyl heptane-3 : 3 : 5 : 5-tetracarboxylate was similarly prepared : one fractional distillation and three crystallisations from light petroleum (b. p. 40—60°) gave the pure ester (33% yield), m. p. 60—61°, b. p. 194°/4 mm. (Found : C, 58·6; H, 8·2. Calc. for $C_{19}H_{32}O_8$: C, 58·7; H, 8·3%). The αα′-dialkylglutaric acids were obtained (96—97% yields) by hydrolysis and decarboxylation of the foregoing esters.[8]

meso-αα′-*Dimethylglutaric Anhydride.*—This was obtained from the mixture of *meso*- and racemic dimethylglutaric acids by the following modification of the method of Auwers *et al.*[2] The acid (1 g.) and acetyl chloride (2 ml.) were allowed to stand in an open tube in warm (50°) water. After the initial vigorous reaction had subsided, the tube was sealed and kept at 100° for 40 hr. The resultant brown liquid deposited a mass of needle-shaped crystals which were collected and, after having been kept *in vacuo* for 2 hr. over potassium hydroxide and phosphoric anhydride, were repeatedly recrystallised from dry ethyl acetate–light petroleum (b. p. 80—100°) to give prisms, m. p. 94—94·5° (yield 40%) (Found : C, 58·9; H, 6·9. Calc. for $C_7H_{10}O_3$: C, 59·1; H, 7·1%).

meso-αα′-*Diethylglutaric Anhydride.*—The *meso*-acid [separated by fractional crystallisation, initially from light petroleum (b. p. 80—100°), and subsequently from water [4b]] formed prisms, m. p. 119—120° (Found : C, 57·0; H, 8·2. Calc. for $C_9H_{16}O_4$: C, 57·4; H, 8·6%). Treatment of this acid with acetyl chloride under reflux for ½ hr. led to an oil, which, when strongly cooled, deposited meso-αα′-*diethylglutaric anhydride* which recrystallised from light petroleum (b. p. 40—60°) in prisms, m. p. 18° (67·4% yield) (Found : C, 63·3; H, 8·1. $C_9H_{14}O_3$ requires C, 63·5; H, 8·3%). It was readily soluble in ether and in benzene.

Preparation of Derivatives.—(i) *Amic acids.* Dry ammonia was passed into a solution of the anhydride (0·45 g.) in about forty times its weight of dry ether. The ether and excess of ammonia were removed. A solution of the residue in water (1 ml.) was acidified with 2N-hydrochloric acid. The clear solution was evaporated *in vacuo* at room temperature and the residue was powdered, dried, and exhaustively extracted with warm dry ethanol (5 × 5 ml.). The combined extracts were filtered, evaporated to 10 ml., and mixed with hot light petroleum (40 ml.; b. p. 80—100°). Two recrystallisations of the precipitated material yielded the pure amic acid.

(ii) N-*Phenyl- and* N-p-*chlorophenyl-glutaramic acids.* The freshly distilled amine (0·0017 mole) was added to a solution of the anhydride (0·0017 mole) in dry chloroform (10—20 ml.) and the precipitate was collected, washed with dry chloroform, and crystallised from a suitable solvent.

(iii) N-p-*Sulphamoylphenylglutaramic acids.* Equimolecular quantities of the anhydride and of recrystallised sulphanilamide were dissolved in the minimum of dry acetone. The acetone was removed on the steam-bath and the residue was recrystallised.

(iv) N-2-*Pyridylglutaramic acids.* These were prepared by a method similar to that described immediately above, but from recrystallised 2-aminopyridine and dry chloroform as solvent.

(v) N-2-*Thiazolylglutaramic acids.* Equimolecular quantities of the anhydride and of 2-aminothiazole [recrystallised from light petroleum (b. p. 100—120°)] were dissolved in a

[5] Welch, *J.*, 1931, 673.
[6] *Org. Synth.*, Coll. Vol. I, 2nd edn., p. 290.
[7] Dressel, *Annalen*, 1890, **256**, 181.
[8] Auwers and Singhof, *Annalen*, 1896, **292**, 205.

minimum of dry chloroform. The solvent was evaporated and an ethereal solution of the residue was repeatedly extracted with 5% aqueous sodium carbonate solution. The combined aqueous extracts were acidified with 2N-hydrochloric acid, and the products were recrystallised.

Glutaramic acids. $R'NH\cdot CO\cdot CHR\cdot CH_2\cdot CHR\cdot CO_2H$.

No.	R	R′	Solvent for recrystn.	M. p.	Yield (%)
1	Me	H	EtOH–l. p.[c]	130°	26
2	Et	H	,,	130·5	22
3	H	C_6H_5	20% EtOH	127 [a]	14
4	Me	,,	,,	158 [b]	84
5	Et	,,	25% EtOH	133	63
6	H	p-Cl·C_6H_4	90% EtOH	134	41
7	Me	,,	20% EtOH	179	87
8	Et	,,	,,	173·5	61
9	H	p-$NH_2\cdot SO_2\cdot C_6H_4$	40% EtOH	191	24
10	Me	,,	15% EtOH	182	41
11	Et	,,	40% EtOH	191·5	44
12	H	2-Pyridyl	EtOH–l. p.[c]	194·5	48
13	Me	,,	80% EtOH	153	26
14	Et	,,	,,	125·5	25
15	H	2-Thiazolyl	85% EtOH	204	58
16	Me	,,	40% EtOH	176·5	33
17	Et	,,	,,	149	33

		Found (%)					Required (%)				
No.	Formula	C	H	N	Cl	S	C	H	N	Cl	S
1	$C_7H_{13}O_3N$	52·5	8·5	8·7	—	—	52·8	8·2	8·8	—	—
2	$C_9H_{17}O_3N$	58·0	9·3	7·9	—	—	57·7	9·2	7·5	—	—
5	$C_{15}H_{21}O_3N$	68·1	7·8	5·6	—	—	68·4	8·0	5·3	—	—
6	$C_{11}H_{12}O_3NCl$	54·9	5·1	5·7	14·7	—	54·7	5·0	5·8	14·7	—
7	$C_{13}H_{16}O_3NCl$	58·2	5·8	5·3	13·5	—	57·9	6·0	5·2	13·2	—
8	$C_{15}H_{20}O_3NCl$	60·5	6·9	4·4	12·4	—	60·5	6·8	4·7	11·9	—
9	$C_{11}H_{14}O_6N_2S$	46·0	4·9	10·0	—	11·6	46·1	4·9	9·8	—	11·2
10	$C_{13}H_{18}O_6N_2S$	49·9	6·1	9·0	—	9·8	49·7	5·8	8·9	—	10·2
11	$C_{15}H_{22}O_6N_2S$	52·9	6·5	8·3	—	9·6	52·6	6·5	8·2	—	9·4
12	$C_{10}H_{12}O_3N_2$	57·3	5·9	13·3	—	—	57·7	5·8	13·5	—	—
13	$C_{12}H_{16}O_3N_2$	61·1	6 7	11·8	—	—	61·0	6·8	11·9	—	—
14	$C_{14}H_{20}O_3N_2$	63·5	7·8	10·5	—	—	63·6	7·6	10·6	—	—
15	$C_8H_{10}O_3N_2S$	45·1	5·0	12·8	—	15·2	44·9	4·7	13·1	—	15·0
16	$C_{10}H_{14}O_3N_2S$	49·8	5·8	11·8	—	13·5	49·6	5·8	11·6	—	13·2
17	$C_{12}H_{16}O_3N_2S$	53·5	6·6	10·1	—	11·5	53·3	6·7	10·4	—	11·9

[a] Balbiano *et al.*[9] give m. p. 126—127°. [b] Auwers *et al.*[10] give m. p. 157°. [c] Ethanol-light petroleum (b. p. 80—100°).

Antibiotic Properties.—None of the derivatives was active against *M. tuberculosis* H37Rv.(Long's medium with 10% serum) at 1 : 3000, except no. 15 which was, however, inactive at 1 : 9000.

No. 13 at 1 : 5000 completely inhibited the growth (on blood-agar) of *Cory. pyogenes.* Slight activity was shown by some other of the derivatives against this organism and also against *H. parapertussis.*

None of the derivatives showed any significant antiprotozoal or antifungal activity and none (of eleven which were tested) was viricidal.

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[9] Balbiano and Angeloni, *Atti R. Accad. Lincei,* 1904, [5], **13**, 146.
[10] Auwers, Oswald, and Thorpe, *Annalen,* 1895, **285**, 236.

404. *Studies in Pyrolysis. Part IX.* The Pyrolysis of the Model Systems 2-Benzoyloxyethyl and 2-p-Chlorobenzoyloxyethyl Terephthalate, and of Poly(ethylene Terephthalate).*

By R. J. P. Allan, H. V. R. Iengar, and P. D. Ritchie.

2-Benzoyloxyethyl and 2-*p*-chlorobenzoyloxyethyl terephthalate break down in the vapour phase (*ca.* 400—550°) by several competitive routes: (i) various alkyl–oxygen scissions (A^1), yielding benzoic (or *p*-chlorobenzoic) and terephthalic acid, and (ii) disproportionation (D), yielding ethylene dibenzoate (or di-*p*-chlorobenzoate). Secondary breakdowns also occur (R/C^1, A^1/D, A^2, and C^2), as predicted.[1-3] Pyrolysis of poly(ethylene terephthalate) (*ca.* 340—475°) yields end-products all of which are in accordance with the same sequence of reactions.

The pyrolysis of various simple model compounds (*e.g.*, ethylene dibenzoate) has been used [1,2,4] as a basis for predicting in detail the thermal breakdown of poly(ethylene terephthalate). The predictions are now confirmed and extended by the pyrolysis (*ca.* 400—550°) of two larger models, 2-benzoyloxyethyl and 2-*p*-chlorobenzoyloxyethyl terephthalate (I; X = H and Cl respectively). As shown later, additional information can be obtained from the model in which the terminal aromatic rings are labelled by a chlorine atom. It is shown that all the breakdown products predicted by the use of such models can be identified in the pyrolysate (*ca.* 340—475°) from commercial poly(ethylene terephthalate).

(I) $$p\text{-X}\cdot C_6H_4\cdot CO_2\cdot \underset{a}{CH_2}\cdot \underset{b}{CH_2}\cdot O_2C\cdot \underset{p}{C_6H_4}\cdot CO_2\cdot \underset{b'}{CH_2}\cdot \underset{a'}{CH_2}\cdot O_2C\cdot C_6H_4\cdot X\text{-}p$$

The following eleven products are formed from the diester (I; X = H or Cl) and the polyester itself: Benzoic and terephthalic acid, acetophenone, *p*-acetylbenzoic acid, acetaldehyde, acid anhydrides, carbon monoxide and dioxide, methane, ethylene, and acetylene. In addition, the diester (I; X = H) yields ethylene dibenzoate, vinyl benzoate, and benzene, while its chloro-derivative (I; X = Cl) also yields *p*-chlorobenzoic acid, *p*-chloroacetophenone, and ethylene di-*p*-chlorobenzoate.

The previous work of Allan, Forman, and Ritchie [2] provides an explanation for all these products. The ester (I) possesses two non-equivalent sets of β-hydrogen atoms; and the predominating primary breakdowns will be alkyl–oxygen scission (A^1) at points *a* or *b*, or at both competitively, thus:

(I) $\underset{a}{\quad}\quad\underset{b}{\quad}\quad\underset{b'}{\quad}\quad\underset{a'}{\quad}$

→ $X\cdot C_6H_4\cdot CO_2H + CH_2{:}CH\cdot O_2C\cdot C_6H_4\cdot CO_2\cdot CH_2\cdot CH_2\cdot O_2C\cdot C_6H_4\cdot X$ (II) . A^1 (point *a*)

→ $X\cdot C_6H_4\cdot CO_2\cdot CH{:}CH_2 + HO_2C\cdot C_6H_4\cdot CO_2\cdot CH_2\cdot CH_2\cdot O_2C\cdot C_6H_4\cdot X$ (III) . A^1 (point *b*)

Thereafter, further alternative or competitive A^1 scissions of esters (II) and (III) can be predicted:

(II) $\underset{b}{\quad}\quad\underset{b'}{\quad}\quad\underset{a'}{\quad}$

→ $CH_2{:}CH\cdot O_2C\cdot C_6H_4\cdot CO_2\cdot CH{:}CH_2 + HO_2C\cdot C_6H_4\cdot X$ . . . . . A^1 (point *a'*)

→ $CH_2{:}CH\cdot O_2C\cdot C_6H_4\cdot CO_2H + CH_2{:}CH\cdot O_2C\cdot C_6H_4\cdot X$ . . . . . A^1 (point *b'*)

(III) $\underset{b}{\quad}\quad\underset{b'}{\quad}\quad\underset{a'}{\quad}$

→ $HO_2C\cdot C_6H_4\cdot CO_2\cdot CH{:}CH_2 + HO_2C\cdot C_6H_4\cdot X$ . . . . . A^1 (point *a'*)

→ $HO_2C\cdot C_6H_4\cdot CO_2H + CH_2{:}CH\cdot O_2C\cdot C_6H_4\cdot X$ . . . . . A^1 (point *b'*)

* Part VIII, *J.*, 1957, 524.

[1] Allan and Ritchie, *Chem. and Ind.*, 1953, 747.
[2] Allan, Forman, and Ritchie, *J.*, 1955, 2717.
[3] Allan, Jones, and Ritchie, *J.*, 1957, 524.
[4] Iengar and Ritchie, *J.*, 1956, 3563.

As each vinyl carboxylate is formed, it will undergo some measure of competitive breakdown by the R/C^1, A^2, and C^2 routes established previously;[2] for example, methyl ketones should be formed as end products, thus:

$$X\cdot C_6H_4\cdot CO_2\cdot CH{:}CH_2 \longrightarrow X\cdot C_6H_4\cdot COMe \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad R/C^1$$

$$HO_2C\cdot C_6H_4\cdot CO_2\cdot CH{:}CH_2 \longrightarrow HO_2C\cdot C_6H_4\cdot COMe \quad . \quad . \quad . \quad . \quad . \quad R/C^1$$

$$CH_2{:}CH\cdot O_2C\cdot C_6H_4\cdot CO_2\cdot CH{:}CH_2 \longrightarrow MeCO\cdot C_6H_4\cdot COMe \quad . \quad . \quad . \quad . \quad . \quad 2(R/C^1)$$

With the exception of the last product, *p*-diacetylbenzene (see Discussion), all the predicted end-products are observed on pyrolysis of the esters (I; X = H or Cl), and of poly(ethylene terephthalate) itself.

Discussion

If compounds (I), (II), and (III) severally undergo, in fact, two competitive A^1 scissions, the overall breakdown scheme of the models is very complex. Almost every end-product can be accounted for in more than one way, and is therefore not diagnostic of a single route only. In practice the multiplicity of β-hydrogen atoms in each model virtually precludes a completely selective A^1 scission at each stage. Some of the alternative sources of particular products are discussed below, both for the model systems and for poly(ethylene terephthalate) itself.

Source of Benzoic Acid.—The ester (I; X = H) could formally yield benzoic acid either by A^1 scission at points *a*, *a'*, or by semidecarboxylation of the terephthalic acid produced by A^1 scission at *b*, *b'*. Since the ester (I; X = Cl) yields much *p*-chlorobenzoic acid and very little benzoic acid, it appears that semidecarboxylation of terephthalic acid is a very minor reaction in the pyrolysis of an ester (I).

Source of Ethylene Dibenzoate.—This compound may formally arise during pyrolysis of the ester (I; X = H) either by decarboxylation (C^2) of the acid (III; X = H) or by the following disproportionation (*D*) of the parent model by ester interchange:

$$2\,X\cdot C_6H_4\cdot[CO_2\cdot CH_2\cdot CH_2\cdot O_2C\cdot C_6H_4]_{(m+n)/2}\cdot X \longrightarrow \left\{\begin{array}{l} X\cdot C_6H_4\cdot[CO_2\cdot CH_2\cdot CH_2\cdot O_2C\cdot C_6H_4]_m\cdot X \\ \qquad + \\ X\cdot C_6H_4\cdot[CO_2\cdot CH_2\cdot CH_2\cdot O_2C\cdot C_6H_4]_n\cdot X \end{array}\right. \quad . \quad D$$

For the model compound (I), $m + n = 4$, and the *D* products will have $m = 1$ (*i.e.*, ethylene dicarboxylate) and $n = 3$. The *D* process may continue further: for example, the larger of the two initial products may now be considered as having $m + n = 6$, and could yield two pairs of products, with $m = 1$, $n = 5$, and $m = 2$, $n = 4$. (It is doubtful whether the larger molecules produced in each *D* reaction will persist in the pyrolysate; they will tend to break down by A^1 scission.) Hence, whatever the degree of disproportionation of the ester (I; X = H), ethylene dibenzoate will be formed; but, since X = H, it is here impossible to discriminate between A^1/C^2 and *D* as the route leading to it. However, the model (I; X = Cl), in which the terminal aromatic rings are labelled by chlorine, yields the corresponding product ethylene di-*p*-chlorobenzoate but not ethylene dibenzoate; here, therefore, the former diester can have arisen from the parent model by the *D* route only. The absence of ethylene dibenzoate simultaneously rules out the alternative possibility that the di-*p*-chlorobenzoate might have arisen less directly from the acid (III; X = Cl) by successive C^2 and *D* reactions; furthermore, there was no sign of the acid (III; X = Cl), or of its decarboxylation product 2-benzoyloxyethyl *p*-chlorobenzoate.

It is clear from this result that a process of continual ester-interchange will proceed in molten poly(ethylene terephthalate) during its pyrolysis.

Source of Acid Anhydrides and Acetaldehyde.—It has been shown[3] that consecutive A^1

and *D* reactions are responsible for the formation of benzoic anhydride and acetaldehyde in the pyrolysis of ethylene dibenzoate :

$$\begin{aligned} \text{BzO·CH}_2\text{·CH}_2\text{·OBz} &\longrightarrow \text{BzOH} + \text{BzO·CH:CH}_2 \quad \ldots\ldots\ldots\ A^1 \\ &\rightleftharpoons \text{BzO·CHMe·OBz} \\ &\longrightarrow \text{Bz}_2\text{O} + \text{Me·CHO} \quad \ldots\ldots\ldots\ D \end{aligned}$$

Precisely the same A^1/D mechanism can explain the formation of acid anhydrides and acetaldehyde from (I), and also [5,6] from poly(ethylene terephthalate). As random scission [5,6] of the polyester chain proceeds, collision and interaction between carboxyl and vinyl ester end-groups will occur more frequently as the individual molecules become smaller and more mobile; and this mobility will be assisted by continual ester-interchange in the molten polyester. (There are, of course, other ways in which acetaldehyde can be formed on pyrolysis of the polyester.[4,7])

Source of Methyl Ketones.—Both for the model (I) and for poly(ethylene terephthalate), many of the vinyl ester end-groups formed by primary A^1 scission will be destroyed by the foregoing secondary A^1/D process : [3]

$$\sim\!\!\sim\text{C}_6\text{H}_4\text{·CO}_2\text{·CH:CH}_2 + \text{HO}_2\text{C·C}_6\text{H}_4\sim\!\!\sim \xrightarrow{-\text{Me·CHO}} \sim\!\!\sim\text{C}_6\text{H}_4\text{·CO·O·OC·C}_6\text{H}_4\sim\!\!\sim$$

Nevertheless, sufficient must survive long enough to allow the R/C^1 process to operate. The acetophenone produced from the ester (I; X = H) may formally arise both by R/C^1 breakdown of vinyl benzoate [1,2] and by decarboxylation of the *p*-acetylbenzoic acid produced from vinyl hydrogen terephthalate by the R/C^1 reaction. However, the former route must predominate strongly because *p*-chloroacetophenone is present in much greater amount than acetophenone in the pyrolysate from the chloro-ester (I; X = Cl), and because *p*-acetylbenzoic acid, pyrolysed for as long as 10 min. at *ca.* 500° in the semimicro-apparatus described by Bain and Ritchie,[8] is decarboxylated to the extent of only *ca.* 25%.

If the competitive A^1 scissions of the polyester chain are truly random, as indicated by the work of Pohl [5] and of Marshall and Todd,[6] terephthalic acid and its mono- and di-vinyl ester should initially be formed in roughly equivalent amounts. Nevertheless, though the acid is a major product in the pyrolysis of both model (I) and the polyester itself, *p*-acetylbenzoic acid [expected to arise from the diester (I) *via* vinyl hydrogen terephthalate, by R/C^1 breakdown, and from the polymer by one or more predictable routes] is observed in small amounts only, and is detectable with difficulty; and *p*-diacetylbenzene [expected to arise from the diester (I) *via* vinyl terephthalate, by two successive R/C^1 changes, and from the polymer by similar predictable routes] could not be detected at all, though very carefully sought. Either, therefore, the diketone is produced in amounts too small to be detected (owing to predominating destruction of its precursor by the A^1/D reaction), or the R/C^1 breakdown of one vinyl ester group so modifies the electronic structure of the (unsymmetrical) product, vinyl *p*-acetylbenzoate, that the second vinyl ester group breaks down preferentially by one of the other competitive routes. The former explanation seems the more probable.

An interesting minor product has been obtained by fractionation of the pyrolysate (liquid phase; *ca.* 340°) from the polyester. It was too small in amount for rigorous purification; but all its chemical properties point to the constitution

$$\text{MeCO·C}_6\text{H}_4\text{·CO}_2\text{·CH}_2\text{·CH}_2\text{·O}_2\text{C·C}_6\text{H}_4\text{·CO}_2\text{H}$$

which is perfectly in accordance with the postulated overall scheme of decomposition.

All the model compounds used in this work have been pyrolysed in the vapour phase, and caution is required in applying the results to predict the breakdown of poly(ethylene

[5] Pohl, *J. Amer. Chem. Soc.*, 1951, **73**, 5660.
[6] Marshall and Todd, *Trans. Faraday Soc.*, 1953, **49**, 67.
[7] Iengar and Ritchie, unpublished observations, 1956.
[8] Bain and Ritchie, *J.*, 1955, 4407.

terephthalate) in the liquid phase. Nevertheless, the present results show that the predictions are justified. When the polyester is pyrolysed in the liquid phase (*ca.* 340°), all the products are explicable on the lines discussed; and there is a large residue of material which is still polymeric, though of reduced molecular weight and increased solubility in phenol. When, on the other hand, molten polyester is fed (at *ca.* 450—475°) into the vapour-phase reaction vessel used for the model compounds, so as to simulate vapour-phase conditions as nearly as possible, breakdown is almost complete, and all the predicted products (except *p*-diacetylbenzene) are observed.

Experimental

Apparatus.—The model compounds (I; X = H or Cl) were pyrolysed in the vapour-phase as previously described,[2] in reactors of various sizes giving a range of different contact times (see Table). Poly(ethylene terephthalate) was pyrolysed (i) by running the molten polyester into a vapour-phase reaction vessel, and also (ii) by heating it under nitrogen in a 3-necked Quickfit flask, enclosed in an electric heating mantle, and fitted with thermometer pocket, cold trap, and balanced aspirator for collecting the exit gases. *p*-Acetylbenzoic acid was pyrolysed in the semimicro-apparatus described previously.[8]

Analytical Methods: Results.—The Table summarises the chief experimental conditions for 8 pyrolyses. Gas analyses are reported on a nitrogen-free basis. Contact times are calculated as previously.[3]

Normal chemical examination of pyrolysate fractions (*a*) and (*b*) (Table) was frequently supplemented by infrared spectrometry and paper chromatography. Carbonyl compounds were identified as their 2 : 4-dinitrophenylhydrazones, either by mixed m. p. or by the paper-chromatographic technique described by Burton.[9] All other solid materials were identified by mixed m. p. Acid anhydrides were detected by the Davidson–Newman colour reaction.[10]

2-Benzoyloxyethyl Terephthalate (I; X = H).—*Preparation.* Sodium terephthalate and 2-chloroethyl benzoate (molar ratio 1 : 2) were heated under reflux with a little diethylamine (200°; 5 hr.; rapid stirring). The product, extracted with benzene and recrystallised from methanol–ethanol, yielded *2-benzoyloxyethyl terephthalate* (31%) as colourles needles, m. p. 114—115° [Found: C, 67·7; H, 4·9%; *M* (cryoscopic in benzene), 471. $C_{26}H_{22}O_8$ requires C, 67·6; H, 4·8%; *M*, 462]. It shows major infrared absorption bands at *ca.* 1780 *s*, 1365 *m*, 1305 *s*, 1145 *s*, 1050 *w*, 996 *w*, 865 *w*, 840 *m*, and 702 *m* cm.$^{-1}$. This compound was also prepared independently and simultaneously in the Blackley Laboratories of Imperial Chemical Industries Limited, Dyestuffs Division.

Pyrolysis of esters (I; X = H *and* Cl) *and poly(ethylene terephthalate).*

Pyrolysand	(I; X = H)				(I; X = Cl)		Polyester	
Pyrolysis no.	1	2	3	4	5	6	7	8
Temp.	500°	500°	400°	500°	500°	525—550°	450—475°	340°
Feed rate (g./min.)	0·54	0·50	0·40	0·70	1·03	1·03	0·67	†
Contact time (sec.)	24	44	63	15	125	115	—	†
Wt. pyrolysed (g.)	66	100	50	50	65	51·5	50	100
(*a*) In cold trap (g.)	2	3	1	—	1	Nil *	5	5
(*b*) In main receiver (g.)	37	58	39	42·5	47	25	17	>84 ‡
(*c*) Gaseous pyrolysate (l.)	6	12·5	2	4·5	4	6·9	9	1
Composition (%) of (*c*):								
CO	—	53·4	48·7	53·3	65·6	54·0	45·6	70·5
CO_2	—	42·7	43·5	40·0	27·7	44·7	47·8	24·9
Sat. hydrocarbons	—	Nil	Nil	Nil	Nil	Nil	Trace	Nil
Unsat. hydrocarbons	—	3·9	7·8	6·7	6·7	1·3	6·6	4·6

* Acetaldehyde vapour removed by 2 : 4-dinitrophenylhydrazine trap before reaching cold trap. † Pyrolysed in static system (5 hr.). ‡ A little of the sublimate could not be scraped out of the vessel. Dashes (—) imply items not examined. Note: There were overall losses due to carbonisation in the reaction vessel.

Pyrolysis 1. The liquid (*a*) in the cold trap contained acetaldehyde; there was no keten (aniline–ether trap). The total pyrolysate was treated with ether; the insoluble residue

[9] Burton, *Chem. and Ind.*, 1954, 576.
[10] Davidson and Newman, *J. Amer. Chem Soc.*, 1952, **74**, 1515.

contained unchanged ester (I; X = H) and terephthalic acid, and the ethereal solution gave benzoic acid (12 g.) by means of an alkaline wash.

The remaining ethereal solution, distilled, yielded (i) 4 g., b. p. 70—100°/2 mm., and (ii) 2 g., b. p. 116—160°/1 mm. Fraction (i) consisted of vinyl benzoate and acetophenone (infrared); these were also present (traces) in fraction (ii), along with benzoic acid. The reaction vessel contained much carbonised matter.

Pyrolysis 2. The liquid (*a*) in the cold trap contained benzene (characterised as *m*-dinitrobenzene) and acetaldehyde. Product (*b*) yielded (i) 5 g., b. p. 75—86°/4 mm., (ii) 4·5 g., b. p. 86—92°/2 mm., (iii) 15 g., b. p. 92—120°/2 mm., and (iv) a solid residue. Fractions (i)—(iii) were similar to the corresponding fractions from pyrolysis 1; fraction (iii) contained a little acetophenone; residue (iv) contained unchanged ester (I; X = H) and terephthalic acid, and on ether-extraction yielded ethylene dibenzoate. There was much carbonised matter.

Pyrolysis 3. The ester (I; X = H) employed was here recrystallised from benzene instead of ethanol–methanol, to ensure that any acetaldehyde formed came from the ester itself and not from any traces of residual alcohol. The liquid (*a*) was mainly acetaldehyde; product (*b*) yielded (i) 1 g., b. p. 100—114°/6 mm. (vinyl benzoate and acetophenone; infrared), and (ii) 1 g., b. p. 114—120°/6 mm. (benzoic acid). The distillation residue (*ca.* 37 g.) was shaken with ether and aqueous potassium carbonate, and filtered; the insoluble residue (14 g.) consisted of unchanged ester (I; X = H) and potassium terephthalate; the aqueous layer, acidified, yielded benzoic acid (14 g.) and terephthalic acid (1 g.); the ethereal layer, on evaporation, yielded a solid (9 g.) which on recrystallisation gave ethylene dibenzoate (mixed m. p.) and a residue containing benzoic anhydride (colour reaction [10]).

Pyrolysis 4. Product (*b*) was shaken with ether and filtered; a 2 : 4-dinitrophenylhydrazone, prepared from the ethereal extract, was examined chromatographically,[9] control "spots" of the 2 : 4-dinitrophenylhydrazones of acetophenone and *p*-acetylbenzoic acid being applied. Elution with acetone (20%) in light petroleum (b. p. 60—80°) resolved the "unknown" spot into two well-defined spots corresponding exactly in position to those from two controls. There was in addition a faint spot, midway between the other two; this did not correspond to any known carbonyl compound, but is presumably due to another of the possible methyl ketones from the pyrolysis. (Pyrolyses 1—3 gave no evidence for the presence of *p*-acetylbenzoic acid; this could be demonstrated only when the Burton method [9] was applied.)

2-*Chloroethyl* p-*Chlorobenzoate*.—*Preparation*. Ethylene chlorohydrin and *p*-chlorobenzoyl chloride (molar ratio 1 : 1), heated at 100° for 2 hr., yielded pure *ester* (77%), m. p. 40°, b. p. 145°/5 mm. (Found: C, 49·6; H, 3·9; Cl, 32·0. $C_9H_8O_2Cl_2$ requires C, 49·3; H, 3·7; Cl, 32·4%).

2-*Hydroxyethyl Terephthalate*.—*Preparation*. Sodium terephthalate and ethylene chlorohydrin (molar ratio 1 : 6) were heated under reflux with a little diethylamine (140°; 24 hr.). Sodium salts were filtered off; the filtrate slowly deposited the crude hydroxy-ester (13%), which yielded 2-*hydroxyethyl terephthalate* as plates, m. p. 112°, from acetone (Found: C, 56·7; H, 5·6. $C_{12}H_{14}O_6$ requires C, 56·7; H, 5·5%). This compound was also prepared independently and simultaneously in the Blackley Laboratories of Imperial Chemical Industries Limited, Dyestuffs Division.

2-p-*Chlorobenzoyloxyethyl Terephthalate* (I; X = Cl).—*Preparation* (a). Sodium terephthalate and 2-chloroethyl *p*-chlorobenzoate (molar ratio 1 : 2·5) were heated under reflux (200°) with a little diethylamine for 6 hr., tetralin being added as a neutral diluent. The product was poured into water and extracted repeatedly with chloroform; removal of chloroform from the extract yielded tetralin with the crude chloro-ester (20%) in suspension. The latter, decolorised with Norit–methanol, yielded 2-p-*chlorobenzoyloxyethyl terephthalate* as fine needles, m. p. 140°, from methanol (Found: C, 59·1; H, 4·1. $C_{26}H_{20}O_8Cl_2$ requires C, 58·8; H, 3·8%).

Preparation (b). 2-Hydroxyethyl terephthalate, *p*-chlorobenzoyl chloride, and pyridine (molar ratio 1 : 2 : 6) were warmed together; the product, poured into water, yielded the crude chloro-ester (*ca.* 100%) as a yellowish solid. This was filtered off and washed successively with dilute hydrochloric acid, aqueous sodium hydrogen carbonate, and water; recrystallisation from ethanol yielded pure ester (I; X = Cl), with properties as above.

Pyrolysis 5. In this trial run, the pyrolysate contained *p*-chlorobenzoic acid, a neutral solid, acid anhydride (colour reaction [10]), and a little acetaldehyde. The total pyrolysate yielded a 2 : 4-dinitrophenylhydrazone, which when chromatographed (circular Whatman No. 3

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paper) and developed with aqueous ethanol gave four rings, showing the presence of four carbonyl compounds other than acetaldehyde.

Pyrolysis 6. The cold trap (*a*) contained acetaldehyde. The total non-gaseous pyrolysate (*b*), triturated with alkali and extracted with ether, yielded (i) an ether extract, (ii) an insoluble solid (1 g.) from the interface, and (iii) an alkaline layer which on acidification yielded a pale yellow solid. The latter gave a 2 : 4-dinitrophenylhydrazone; when chromatographed,[9] this gave a spot corresponding precisely (control) to the derivative from *p*-acetylbenzoic acid. 5 g. of (iii), treated with chloroform, gave 1 g. of an insoluble mixture of *p*-chlorobenzoic and terephthalic acid (infrared); the chloroform extract yielded a mixture of benzoic and *p*-chlorobenzoic acid (chromatography). Extract (i) yielded a liquid (22·7 g.) which solidified overnight. A 5 g. sample of this was macerated with light petroleum (20 ml.; b. p. 80—100°) and then warmed with a further 20 ml. of the same solvent; an upper layer (decanted from a lower layer of insoluble oil) yielded, on cooling, ethylene di-*p*-chlorobenzoate (0·6 g.), as prismatic rods, m. p. 133—139° (from ethanol) (mixed m. p. and infrared). Extract (i) also yielded a bright red 2 : 4-dinitrophenylhydrazone; this was chromatographed [11] on bentonite–kieselguhr (4 : 1), development being first with chloroform and working up to acetone. The eluate was collected in 10 ml. samples, and the separation followed by plotting optical density (Spekker; blue filter) against fraction number. Five well-defined maxima were recorded. The first two corresponded (chromatography [9]) to acetophenone and *p*-chloroacetophenone respectively; the other three (lower R_F values) remain unattributed, but very probably correspond to methyl ketones of higher complexity and molecular weight (cf. pyrolysis 5).

Poly(ethylene Terephthalate).—Carefully dried "Terylene" flake was used. In a trial pyrolysis, 10—20 g. samples were heated for 2 hr. under nitrogen in conical flasks immersed in a Wood's-metal bath; no decomposition was observed below 190°, but at 210—220° a white acidic sublimate was formed.

Pyrolysis 7. The cold trap (*a*) contained acetaldehyde. Pyrolysate (*b*), which contained acid anhydride (colour test [10]), was refluxed with ether (100 ml.) and gave a residue (2 g.) of terephthalic acid (infrared). The ether extract, washed with water and with aqueous alkali, and then dried, yielded a yellow liquid (1 g.) containing traces of suspended solid; it was mainly vinyl benzoate (infrared) containing some acetophenone (chromatography [9]). The aqueous extracts, when acidified, gave a yellowish solid (10 g.); this yielded a fraction soluble in hot water (mostly benzoic acid, but yielding also a trace of a 2 : 4-dinitrophenylhydrazone), an ethanol–soluble fraction containing *p*-acetylbenzoic acid (chromatography [9]), and an insoluble residue of terephthalic acid (infrared). The gaseous pyrolysate (*c*) contained carbon monoxide and dioxide, methane, ethylene, and acetylene (infrared).

Pyrolysis 8. The cold trap (*a*) contained acetaldehyde (5 g.) and no vinyl ether (infrared); there was a solid sublimate (*ca.* 14 g.) and a dark intractable solid residue (70 g.). The sublimate was boiled with water (100 ml.); the filtrate yielded benzoic acid on cooling; the residue was warmed with ethanol (100 ml.), yielding an insoluble residue of terephthalic acid (infrared) and a filtrate. A portion of the latter gave a 2 : 4-dinitrophenylhydrazone which formed two spots (chromatography [9]), one unknown and one corresponding to acetophenone; the remainder, on concentration, yielded a white solid *A*, m. p. >360°, and a filtrate which gave the 2 : 4-dinitrophenylhydrazone of acetophenone only.

64 g. of the dark tarry residue from the reaction vessel were treated with boiling acetone (400 ml.), yielding (i) a filtrate and (ii) an acetone-insoluble residue, more soluble in phenol than was the original polyester. On hydrolysis, fraction (ii) yielded ethylene glycol (characterised as its dibenzoate) and crude terephthalic acid (infrared); quantitative saponification gave 87·9% of terephthalic acid (Calc. for repeat-unit $[CH_2{\cdot}CH_2{\cdot}O_2C{\cdot}C_6H_4{\cdot}CO_2]$: 86·4%). It thus appears that fraction (ii) is essentially a lower poly(ethylene terephthalate), the slightly high acid-content probably indicating the presence of some random anhydride linkages. The soluble fraction from filtrate (i) was separated by cold alkali into two sub-fractions, terephthalic acid and a solid with m. p. >350°, apparently identical with *A*.

Substance *A* dissolved in hot (but not cold) caustic alkali or sodium hydrogen carbonate; back-titration gave the titration equivalent (E_t), and addition of excess of acid regenerated *A*. Complete alkaline hydrolysis measured the saponification equivalent (E_s) and liberated terephthalic acid and ethylene glycol; the latter was determined (G%) by the periodic acid method. Attempts to determine molecular weight by the Rast method in camphor gave

[11] Elvidge and Whalley, *Chem. and Ind.*, 1955, 589.

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erratic and unreliable results. The substance was contaminated by a trace of *p*-acetylbenzoic acid (paper chromatography [9]) which could not be removed from the very small sample available; the following analytical data cannot, therefore, be considered as rigorously accurate, but point fairly conclusively to the constitution (IV; X = Ac, $n = 0$), 2-*p*-acetylbenzoyloxyethyl hydrogen terephthalate.

(IV) $X{\cdot}C_6H_4{\cdot}CO_2{\cdot}CH_2{\cdot}CH_2{\cdot}[O_2C{\cdot}C_6H_4{\cdot}CO_2{\cdot}CH_2{\cdot}CH_2]_n{\cdot}O_2C{\cdot}C_6H_4{\cdot}CO_2H$

The analytical data were compared with figures calculated for 12 different variations of the above formula (X = H, CO_2H, Ac: $n = 0, 1, 2, 3$); but for no other case was there good agreement [Found: C, 63·9; H, 4·7%; E_t, 361·9; E_s, 121·6, 123·8; *G*, 17·1%. $C_{19}H_{16}O_7$ (IV; X = Ac, $n = 0$) requires C, 63·9; H, 4·5%; E_t, 356; E_s, 118·7; *G*, 17·4%]. Attempts to detect *p*-acetylbenzoic acid in the total hydrolysate from *A* are meaningless, since the ketonic acid is originally present as a trace impurity.

p-*Acetylbenzoic Acid.—Preparation.* The acid, prepared by standard methods,[12,13] had m. p. 200° (lit.,[13] 200°,[14] 208°).

Pyrolysis of p-*Acetylbenzoic Acid.*—In a semimicro-apparatus [8] (500°; 10 min.) 0·3 g. of acid evolved a gaseous pyrolysate (CO, 17·6; CO_2, 82·4%) containing 10·5 ml. of carbon dioxide, indicating 25·6% of decarboxylation. Examined by the nitroprusside test [15] for methyl ketones, the liquid residue gave a much stronger reaction than the original acid itself (checked by control mixtures); the odour of acetophenone was apparent.

p-*Diacetylbenzene.—Preparation.* The diketone was prepared from *p*-ethylacetophenone; [16] treatment with a large excess of 2 : 4-dinitrophenylhydrazine yielded a product which, even after several recrystallisations (glacial acetic acid) gave on chromatography [9] two resolved spots, presumably corresponding to mono- and di-2 : 4-dinitrophenylhydrazones. The recrystallised but unresolved mixture was used in testing pyrolysates chromatographically for the presence of *p*-diacetylbenzene.

Ethylene Di-p-*chlorobenzoate.—Preparation.* Ethylene glycol and *p*-chlorobenzoyl chloride (molar ratio 1 : 1), warmed in pyridine, yielded the diester, m. p. 142—143°, from ethanol (lit.,[17] 140°) (Found: Cl, 20·5. Calc. for $C_{16}H_{12}O_4Cl_2$: Cl, 20·9%).

[*Added March 8th*, 1957.] Since this paper was written, it has come to our notice that the preparation of 2-hydroxyethyl terephthalate has previously been recorded.[18] It is described as having m. p. 109° (from water).

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[12] Raadsveld, *Rec. Trav. chim.*, 1935, **54**, 815.
[13] Ahrens, *Ber.*, 1887, **20**, 2956.
[14] Fichter and Meyer, *Helv. Chim. Acta*, 1925, **8**, 285.
[15] Bitto, *Annalen*, 1892, **267**, 372.
[16] Hochwalt, U.S.P. 2,390,368/1945.
[17] Heim and Poe, *J. Org. Chem.*, 1944, **9**, 299.
[18] Zahn and Krzikalla, *Angew. Chem.*, 1955, **67**, 108; cf. Farthing, B.P. 623,669/1947, G.P. 905,736/1954.

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405. *The Preparation and Properties of Some Organomercury Groups.*

By B. G. Gowenlock and J. Trotman.

Organomercury groups (RHg) are prepared as cathode deposits on electrolysis of organomercuric chlorides in liquid ammonia. Decomposition temperatures of the groups and decomposition voltages for the electrolyses are measured. Decomposition of the groups in the presence of free-radical detectors suggests the absence of free radicals in the groups. Previous discussions of the chemical character of the groups are reviewed, and their properties described in terms of the Pauling theory of metals. Evidence for the existence of similar organometallic groups is reviewed, and suggestions made for the preparation of possible analogues.

The term " organomercury group " is used to described the free groups first prepared by Kraus [1] and considered by him to be solid free radicals.[2] Kraus prepared CH_3·Hg, C_2H_5·Hg, and n-C_3H_7·Hg as black deposition products on the cathode by electrolysis of the corresponding alkylmercuric chlorides in liquid ammonia at temperatures between $-60°$ and $-34°$, platinum wire electrodes being employed. Kraus established that the groups decomposed on warming to " very near ordinary temperatures " according to the equation $2RHg \longrightarrow R_2Hg + Hg$. Attempts to electrolyse the n-pentyl- and n-octyl-mercuric iodides gave, respectively, slight and no indication of the existence of the corresponding organomercury groups. Rice and Evering [3] repeated the preparation of CH_3·Hg and observed that the solid would not sublime in a high vacuum at $-20°$ to $-10°$. The substances described by Hein and Mesée [4] are probably the corresponding phenyl- and benzyl-mercury groups: these were prepared by directing the pyrolysis products of benzene and toluene respectively on a stream of mercury vapour condensing on a cold finger, the final products being condensed in a trap cooled in liquid air. The black solids resulting decomposed on warming to room temperature to give mercury and the corresponding diarylmercury. The solids are represented as mercurous aryls and the decomposition expressed as $R_2Hg_2 \longrightarrow R_2Hg + Hg$.

RHg radicals have been postulated as intermediates in the electrolysis of solutions of alkylmercuric compounds,[5,6] where mercury dialkyls are produced in high (≥90%) yields, the reaction being presumably

$$2RHg^+ + 2e \longrightarrow 2RHg \longrightarrow R_2Hg + Hg$$

Similarly, RHg radicals have been postulated as intermediates in the polarographic reduction of some organic and organomercuric halides.[7,8,9]

Experimental

Compounds RHgCl (R = Me, Et, Pr^n, Pr^i, Bu^n, Ph, $PhCH_2$, *trans*-Cl·CH:CH·) were prepared by standard methods.[10,11] A run was carried out by first saturating liquid ammonia with the mercurial at $-78°$. The solution was then displaced into the glass reaction vessel containing an internal sintered-glass filter after the design of Fowles and Pollard,[12] the reaction

[1] Kraus, *J. Amer. Chem. Soc.*, 1913, **35**, 1732.
[2] *Idem*, *Rec. Trav. chim.*, 1923, **42**, 588.
[3] Rice and Evering, *J. Amer. Chem. Soc.*, 1934, **56**, 2105.
[4] Hein and Mesée, *Ber.*, 1943, **76**, 430.
[5] Maynard and Howard, *J.*, 1923, 760.
[6] Melnikov and Rokitskaya, *J. Gen. Chem., U.S.S.R.*, 1937, **7**, 2596.
[7] Benesch and Benesch, *J. Amer. Chem. Soc.*, 1951, **73**, 3391; *J. Phys. Chem.*, 1952, **56**, 648.
[8] Colichman and Maffei, *J. Amer. Chem. Soc.*, 1952, **74**, 2744.
[9] Oldham, Ph.D. Thesis, Manchester, 1952, cited by Pritchard, *Chem. Rev.*, 1953, **52**, 529.
[10] Krause and von Grosse, " Die Chemie der metall-organischen Verbindungen," Borntraeger, Berlin, 1937, p. 129.
[11] Freidlina and Nesmeyanov, *Compt. rend. Acad. Sci. U.R.S.S.*, 1940, **26**, 60.
[12] Fowles and Pollard, *J.*, 1953, 2588.

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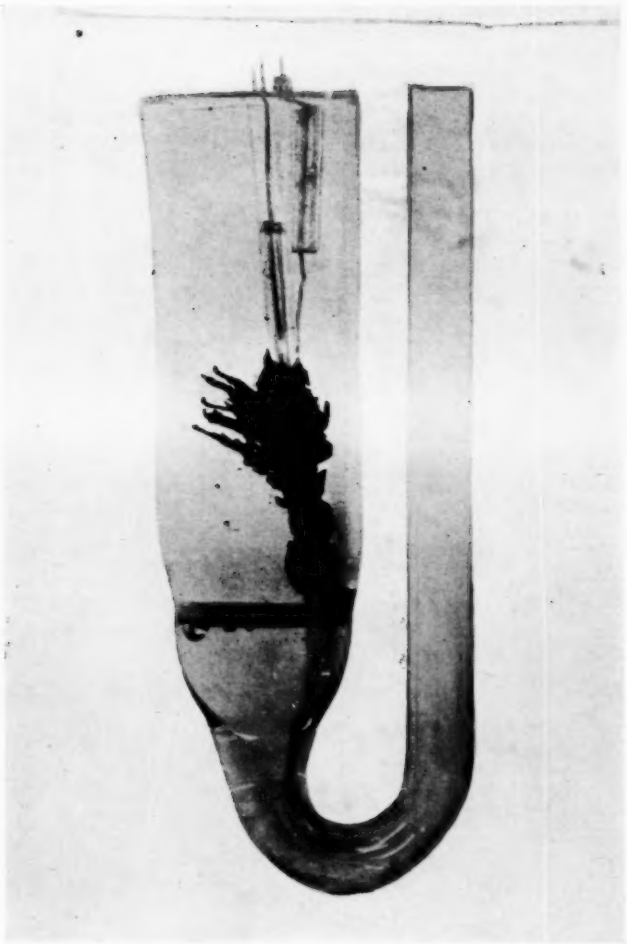

Cathode deposit of n-*butylmercury group formed on electrolysis of* Bu^nHgCl *in liquid ammonia at* $-78°$.

[*To face p.* 2114.

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vessel being cooled to −78° by solid CO_2–acetone. All operations were carried out with exclusion of air and moisture. Two platinum wire electrodes mounted in the centre of the reaction vessel were employed and the solutions were electrolysed at −78°, a potential difference of about 4—6 v being used for most cases; the current passed was 2—10 mA. A deposit, usually black, formed rapidly at the cathods, and a stream of bubbles (presumably chlorine) appeared at the anode. The anode was attacked by the gas liberated thereat, and this necessitated renewal of the electrode after about four runs. In every case, deposition of the solid was accelerated visibly by continued electrolysis. The length of runs varied from 2 to 4 hr. and on completion the solid was filtered off and washed with liquid ammonia or cold (−78°) methanol. The deposit was then continuously pumped under high vacuum to remove traces of ammonia or methanol: in practice, it proved difficult to produce a pressure lower than 0·01 mm. Hg. The decomposition voltage for each electrolysis was measured; the results are in Table 1. The values were reproducible and were unaltered on substitution of a silver-coated cathode.

TABLE 1. *Decomposition voltages of saturated solutions of* RHgCl *in liquid ammonia at* −78°.

R	Me	Et	Pr^n	Pr^i	Bu^n	Ph	$PhCH_2$	Cl·CH:CH·
Decomp. voltage (v)	1·2	1·4	1·75	1·5	1·8	37[a]	-----[b]	0·9[c]

[a] Slowly decreased throughout run, 8v after 3½ hr., 2v after 5 hr.
[b] Considerable fluctuations of current accompanying decomposition of product made determination impossible.
[c] White crystals deposited in solution, mercury deposited at cathode.

The approximate decomposition temperatures of the groups were determined by rapid removal of the groups from the sintered disc to a tube containing ethanol at −78°. The tube and contents were allowed to warm slowly to room temperature and the temperature at which the solid changed rapidly to give mercury globules was determined by means of a pentane thermometer. In no case did the solid melt before decomposition; results are in Table 2.

TABLE 2. *Decomposition temperatures of organomercury groups.*

R	Me	Et	Pr^n	Pr^i	Bu^n	Ph	$PhCH_2$
Decomp. temp.	−10° to −15°	−15° to 0°	−5°	−25°	−5°	−20° to 0°[a]	-----[b]

[a] Solid changes only slightly in appearance on decomposition.
[b] Some decomposition occurs at −78°.

When some of the *iso*propylmercury group was allowed to warm in air whilst attached to the cathode it decomposed with a loud cracking sound.

The groups varied in appearance; the methyl and ethyl groups were black flaky deposits which could be readily detached from the cathode by tapping the vessel or rotating the electrode. The deposits fell from the cathode at short intervals during electrolysis. The *iso*propyl group was very similar in appearance to the methyl and ethyl analogues, but adhered more strongly to the cathode. The *n*-propyl group was a black deposit with a reddish-brown tinge, thin layers being purple: it was softer than the methyl, ethyl, and *iso*propyl analogues, adhered to the cathode, and grew in a tree-like manner. The *n*-butyl group was black, with a reddish-brown tinge which became more intense as electrolysis proceeded: it adhered firmly to the cathode and grew in a tree-like manner (see Plate). The phenyl and benzyl groups were black and dark grey respectively, and the latter adhered firmly to the cathode.

Reactions of the Groups.—Neither the methyl nor the ethyl group changed when kept in the presence of 10 mm. of nitric oxide at −78° for 12 hr. On gradual warming to room temperature, followed by cooling to −78°, there was no change in pressure, indicating that nitric oxide had not been consumed. Ultraviolet spectrophotometric examination of the decomposition products in ethanol solution gave $\lambda_{max.}$ 210 mμ, characteristic of mercury compounds,[13] with no evidence of formation of nitrosoalkanes.[14]

Decomposition of the methylmercury group by warming to room temperature, followed by cooling to −78° and measurement of the pressure (McLeod gauge) gave no pressure rise, indicating absence of volatile hydrocarbons and ammonia in the decomposition products. The

[13] Gowenlock and Trotman, *J.*, 1955, 1454.
[14] *Idem, ibid.*, p. 4190.

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decomposition products of the phenylmercury group when dissolved in ethanol had ultraviolet absorptions characteristic of diphenylmercury,[13] the low intensity of absorption in the 245—250 mμ region indicating very little formation, if any, of diphenyl, which has $\lambda_{max.}$ (in EtOH) 248 mμ, log ε 4·21.

Electrolysis of methylmercuric chloride in the presence of styrene, prolonged contact of the methylmercury group with styrene in liquid ammonia at −45°, and warming the methylmercury group to room temperature in the presence of an ethanolic solution of styrene produced no polystyrene.

An acetone solution of diphenylpicrylhydrazyl gave no observable colour change at −78° during 12 hr. with the ethylmercury group or on warming the group to room temperature. The relative proportions were approximately 1 mole of diphenylpicrylhydrazyl to 100 " moles " of EtHg.

Discussion

The decomposition voltages observed by us are of the same order as those reported by Evans, Lee, and Lee [15] for ethereal solutions of Grignard reagents, which are the only analogous determinations reported in the literature. For Grignard reagents, the variation of decomposition voltage with increase in size of the alkyl group is irregular. The cathodic deposition of mercury and the precipitation of white needles during the electrolysis of *trans*-2-chlorovinylmercuric chloride suggest the occurrence of the reaction

$$2Cl\cdot CH{:}CH\cdot HgCl \longrightarrow HgCl_2 + Hg(Cl\cdot CH{:}CH)_2 \downarrow$$

which can occur in chloroform solution impregnated with gaseous ammonia.[11] Confirmation of this explanation, which implies that electrolysis is confined to the soluble mercuric chloride, is provided by the close agreement of the observed decomposition voltage with that recorded by Groening and Cady [16] for liquid ammonia solutions of mercuric chloride (0·85 v).

Kraus's original observations [1] are confirmed and extended, except that the reddish liquid observed when the ethylmercury group melts (and predicted for the *n*-propylmercury group) was never observed by us. In particular, we have confirmed Kraus's observation that alcoholic solutions of organomercuric halides can be similarly electrolysed at low temperatures to yield the organomercury groups. However, the solubility of the halides is much lower, the decomposition voltages are higher (about 7 v for MeHgCl), and much larger potential differences are necessary (about 100 v) to yield the organomercury groups in any quantity. We have also confirmed that the groups decompose slowly at about −50; such decomposition rendered impossible attempts to measure the resistance of the solid groups and its temperature dependence. The predominant decomposition reaction of the groups is

$$2HgR \longrightarrow Hg + HgR_2$$

and our failure to detect R radicals or R–R products suggests that the reactions

$$HgR \longrightarrow Hg + R\cdot;\ R\cdot + R\cdot \longrightarrow R{-}R$$

can participate to a small extent only.

The organomercury groups can be considered to be (*a*) free radicals, RHg·, (*b*) amalgams of mercury with organic free radicals R·, (*c*) organomercurous compounds R·Hg·HgR, or (*d*) organic " metals." Each of these hypotheses can be evaluated in the light of the experimental evidence.

If the groups are free radicals, it seems likely that they would react with either nitric oxide or diphenylpicrylhydrazyl, or initiate the polymerization of styrene. It is also known that solid free radicals that have no resonance stabilization decompose at temperatures much lower than −20°, *e.g.*, the nitrogen- and sulphur-containing radicals

[15] Evans, Lee, and Lee, *J. Amer. Chem. Soc.*, 1935, **57**, 489.
[16] Groening and Cady, *J. Phys. Chem.*, 1926, **30**, 1597.

listed by Rice [17] which decompose between −195° and −125°. A further argument against the free-radical hypothesis is given by the fact that D(Hg–H) is approximately equal to D(Hg–CH_3),[18] yet the solid of composition HgH decomposes into mercury and hydrogen between −125° and −100°.[19] This observation suggests that whereas the HgH solid may be a free radical, the organomercury group has a non-radical character.

If the groups are 1 : 1 amalgams of mercury and free radicals, it would be expected that further addition of mercury would cause further amalgamation; such behaviour has not been observed by either Kraus [1] or us. The polarographic reduction of RHg^+ at room temperature gives $RHg^{\cdot}$ radicals [7, 8, 9] with resultant dissolution of the radicals in the mercury drop

$$RHg^{\cdot} + Hg \longrightarrow R \text{ (solution in Hg)}$$

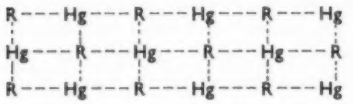
The marked difference in behaviour of the organomercury groups suggests that they are neither radicals nor amalgams. In addition the failure to yield R–R on decomposition suggests that R is not free from bonding of some type with the mercury. The groups are obviously different from the tetramethylammonium amalgam which yields free methyl radicals [20] on decomposition above 0°.

Hein and Mesée [4] implied that the groups were organomercurous compounds R·Hg·HgR, and the close analogy between the decomposition of the groups and inorganic mercurous compounds makes such a hypothesis plausible. It is known that the decomposition temperatures of mercurous halides decrease from chlorine to iodine (*i.e.*, with increase in covalent character) and the presumably covalent mercurous alkyls should have an even lower decomposition temperature. Molten mercurous chloride is red-brown [21] and thus exhibits a similar colour to the *n*-propyl- and the *n*-butyl-mercury groups. It can be further argued that, although mercuric alkyls are undissociated into ions and concentration of mercurous ions will therefore also be negligible ($[Hg_2^{2+}]/[Hg^{2+}] = 116$ in presence of metallic mercury [22]), the disproportionation reaction $Hg_2^{2+} \longrightarrow Hg + Hg^{2+}$ by which the decomposition must occur is considerably retarded by the low temperature, and that the decomposition temperature represents the threshold at which this can occur. However, it seems unlikely that a covalent mercurous bond could exist,[22] and to attribute a large ionic character to a mercurous–carbon bond would be contrary to expectation. A very approximate estimate of the Hg–Hg bond length in "mercurous methyl" can be obtained from a plot of known Hg–Hg bond lengths in mercurous halides [23] against the electronegativity of the halide; [24] extrapolation to zero electronegativity at 3·3 Å (bond length [25] in Hg_2) produces an Hg–Hg distance of 2·75—2·90 Å at electronegativity 2·0—2·1 (cf. Pritchard [9]). This distance corresponds to the expected value for a covalent Hg–Hg bond. The most conclusive argument against the identification of the groups with a mercurous alkyl structure lies in the high electrical conductivity of the solid groups compared with the very high resistances of solid inorganic mercurous compounds.[26]

Kraus implied that the groups were metallic and contained delocalised free electrons; Coates [27] has elaborated this view, considering the groups to be R–Hg^+ ions in a metallic lattice, together with the equivalent number of "free" electrons, *i.e.*, an *organic metal*. The electrical properties of the groups necessitate such an approach, or treatment in terms

[17] Rice, *J. Chem. Phys.*, 1956, **24**, 1259.
[18] Gowenlock, Polanyi, and Warhurst, *Proc. Roy. Soc.*, 1953, *A*, **219**, 270.
[19] Geib and Harteck, *Chem. Ber.*, 1932, **65**, 1550.
[20] Porter, *J.*, 1954, 760.
[21] Klemm and Biltz, *Z. anorg. Chem.*, 1926, **152**, 225.
[22] Sidgwick, "The Chemical Elements and their Compounds," Oxford Univ. Press, 1950, p. 292.
[23] Grdenić and Djordjević, *J.*, 1956, 1316.
[24] Pauling, "The Nature of the Chemical Bond," Cornell University Press, New York, 1940, p. 64.
[25] Syrkin and Dyatkina, "Structure of Molecules and the Chemical Bond," Butterworths, London, 1950, p. 151.
[26] Gowenlock and Trotman, unpublished observations.
[27] Coates, *Quart. Reviews*, 1950, **4**, 217; "Organo-Metallic Compounds," Methuen, London, 1956, p. 47.

of a theory of metals. The existence of an electron-pair bond and a free electron in R:Hg· suggests the possibility of resonance on the pattern of the Pauling theory of metals (ref. 24, p. 401). We can represent the group structure diagrammatically as in (I), each mercury atom being bonded to six organic groups R, the electrons being delocalised throughout the solid. Thus we have a distorted mercury lattice. At low temperatures the structure is reasonably stable, but as the temperature increases, the lattice vibrations become more intense and an HgR_2 molecule is formed as two energetic R groups converge simultaneously and collinearly on the opposite sides of a mercury atom, localisation of electrons resulting. R–R formation is improbable as all R groups are separated from one another by mercury atoms. Such a hypothesis implies that stability of the group depends on the size of R. Thus the relatively small hydrogen atom can diffuse through the mercury rhombohedral lattice, and so the HgH group will possess low thermal stability. When R is large, it can no longer be accommodated by the lattice and hence thermal stability is low. Our observations for R = $PhCH_2$, and those of Kraus [1] for R = *n*-pentyl and *n*-octyl again confirm this hypothesis. We are of the opinion that this approach to the structure of the organomercury groups accords better with the experimental observations than the other suggestions we have examined.



(I)

It is possible that other organometallic groups occur. Hein and Eissner's [28] "chromium polyphenyls" are similar to the organomercury groups in their method of preparation, but have recently been shown to possess ferrocene-type structures.[29] Other possible analogues are the "trimethyltin radical" [30] and dimethylgallium.[31] However, the former is identical with hexamethyldistannane, and the latter reacts rapidly with ammonia. Possible analogues must possess the same capacity for limited distortion of the metal lattice, and probably have an alkyl : metal ratio of 1 : 1. Investigation of the reduction of RZnX, RCdX (as yet unknown), $RAuX_2$, $RTlX_2$, $RPbX_3$, and their analogues (X = halogen) in suitable media at low temperatures is necessary. The zinc and cadmium metallic lattices and interatomic distances are sufficiently similar to the mercury lattice to make preparation of their organometallic groups possible; also the decomposition of these groups would parallel the mercury case. It is possible that the greater thermal stability of RZn and RCd radicals than of RHg radicals [estimated on the assumption that $D(CH_3\text{–}M) \simeq D(H\text{–}M)$[18,32]] implies that the second stage in the reaction sequence

$$RM^{+} + e \longrightarrow RM\ (radical) \longrightarrow (RM)_n\ (group)$$

is less likely to occur. In this case, the organomercury groups may well be unique.

One of us (J. T.) acknowledges a maintenance grant from the D.S.I.R.

UNIVERSITY OF BIRMINGHAM. [*Received, November 19th*, 1956.]

[28] Hein and Eissner, *Ber.*, 1926, **59**, 362.
[29] Cotton, *Chem. Rev.*, 1955, **55**, 551; Fischer and Seus, *Chem. Ber.*, 1956, **89**, 1809.
[30] Kraus and Sessions, *J. Amer. Chem. Soc.*, 1925, **47**, 2361.
[31] Kraus and Toonder, *ibid.*, 1933, **55**, 3547.
[32] Gaydon, "Dissociation Energies," Chapman and Hall, London, 1953, chapter 12.

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406. *Some Physical and Chemical Properties of Vanadium Pentafluoride.*

By H. C. Clark and H. J. Emeléus.

New values for the melting point, vapour pressure, boiling point, and the specific conductivity of vanadium pentafluoride are given. The strength of the pentafluoride as a fluorinating agent has been investigated by a study of its reactions with carbon tetrachloride, tetrabromide, and tetraiodide.

Since the first reported preparation of vanadium pentafluoride [1] it has only once been further studied, when Emeléus and Gutmann [2] prepared it by direct fluorination of the metal at 300° and showed that with metal fluorides it forms hexafluorovanadates of the type MVF_6. The physical properties and simple reactions of vanadium pentafluoride are thus unknown or only known approximately; this is probably due to the difficulty of handling the compound in glass apparatus.

Recent work here [3] has shown that a reactive fluoride such as molybdenum hexafluoride can be prepared and purified and its properties investigated in glass systems from which moisture and vacuum grease have been rigidly excluded. This technique has now been successfully applied to the study of vanadium pentafluoride, allowing the determination of the melting point, vapour pressure, boiling point, and specific conductivity. In view of its great reactivity, vanadium pentafluoride should be an effective fluorinating agent and this property has been investigated by studying the reactions of the pentafluoride with carbon tetrachloride, tetrabromide, and tetraiodide.

Experimental

Vanadium pentafluoride was prepared by direct fluorination [2] of vanadium powder in a nickel boat at 300°. The pale yellow distillate was collected at −183° in glass traps containing sodium fluoride which had been previously heated to 750° to remove all traces of hydrogen fluoride. The traps were connected by capillaries and were fitted with glass break-seals, thus forming systems from which all traces of moisture, hydrogen fluoride, vacuum grease, and other impurities could be rigidly excluded. The impure distillate was purified by trap-to-trap distillation over sodium fluoride in similar all-glass systems, the final product being a white solid which melted slowly at room temperature to a pale yellow viscous liquid.

The molecular weight of vanadium pentafluoride was determined in the apparatus described by O'Donnell [3] in which conventional glass taps were replaced by metal Hoke valves. The mean molecular weight from several determinations was 148·0 (Calc. for VF_5: *M*, 146·0).

Samples of the pentafluoride were analysed by dissolving known weights of the compound in dilute alkali. The vanadium was then determined by reduction with sulphur dioxide and titration with standard potassium permanganate. Fluorine was determined by precipitation as calcium fluoride from samples from which the vanadium had been previously precipitated as the oxine complex; [4] this also confirmed the first vanadium analysis. Thus, the sample used in the determination of the m. p. gave V, 35·15, 34·8; F, 65·3 (Calc. for VF_5: V, 34·9; F, 65·1%).

The melting point, found to be 19·5° ± 0·5°, was determined by Stock's method.[5] Its sharpness, as indicated by the rapid movement of the glass style through the melting material, was a further indication of the purity of the sample.

The vapour pressure of vanadium pentafluoride was determined over the temperature range −20° to +45·5° by means of a sensitive Pyrex spiral gauge which had been thoroughly dried by flaming *in vacuo* and flushing several times with dry air. The pentafluoride was purified by distillation over sodium fluoride and was finally distilled through a capillary into

[1] Ruff and Lickfett, *Ber.*, 1911, **44**, 2539.
[2] Emeléus and Gutmann, *J.*, 1949, 2979.
[3] O'Donnell, *J.*, 1956, 4681.
[4] Montequi and Gallego, *Anales Fis. Quim.*, 1934, **32**, 134.
[5] Stock, *Ber.*, 1917, **50**, 156.

a small bulb attached to the spiral gauge. The capillary was then sealed to provide an all-glass system. The gauge was arranged with as large a distance as possible between the spiral and the reflecting mirror so that for measurements above room temperature all significant parts were adequately immersed in the bath liquid. The difficulties encountered by Fairbrother and Frith [6] in the measurement of the vapour pressures of niobium and tantalum pentafluorides owing to slow hydrolysis are considerably greater in the case of vanadium pentafluoride, which is much more sensitive to oxygen and moisture, so the values tabulated below will be somewhat less reliable. These values were determined with rising temperature, but several were re-determined as the temperature fell, the agreement between the values showing that any reaction with the glass had been negligible.

Temp. (°K)	252	256	263	268	272	275·5	284	286	293	296
Pressure (mm. Hg) ...	5·0	7·5	13·0	20·5	28·5	37·5	71·5	85·0	133·5	178·5
Temp. (°K)	296·5	300	300·5	305	307	308·5	310·5	312	314·5	318·5
Pressure (mm. Hg) ...	182·0	227·0	235·0	311·0	336·0	391·0	440·0	471·0	535·0	659·0

Conductivity was measured by using the apparatus described by Haszeldine and Woolf [7] with a Pyrex cell with circular platinum electrodes approximately 1 mm. apart. For convenience in cleaning, the cell was fitted with a ground-glass joint which was made vacuum tight with a tapered Teflon sleeve. Measurements made at 25—45° gave the following values of the specific conductivity κ:

Temp.	25°	30°	34°	36°	39°	42°	45°
$10^4\kappa$ (ohm^{-1} cm.$^{-1}$)	2·43	3·09	3·86	4·17	4·77	5·44	6·20

These values give a straight-line plot of $\log_{10}(\kappa \times 10^4)$ against $1/T$. Further measurements were made of the conductivity of a sample to which potassium fluoride had been added. However, the solubility of potassium fluoride was much lower than expected, but sufficient to increase the specific conductivity to $8{\cdot}1 \times 10^{-4}$ at 25°.

The reactions of vanadium pentafluoride with carbon tetrachloride, tetrabromide, and tetraiodide were also carried out in systems in which conventional taps and joints were replaced by capillaries and break-seals. The volatile products of each reaction were fractionated through such systems and the various fractions identified by the determination of vapour pressures and molecular weights in the apparatus previously described.[3] Involatile residues were analysed for vanadium and fluorine as described above, and for other elements by standard methods.

Excess of vanadium pentafluoride reacted with carbon tetrachloride (1·50 g.) at room temperature to produce 1·18 g. of trichlorofluoromethane (Found: M, 137·7. Calc. for CCl_3F: M, 137·5). Secondary products were a yellow gaseous mixture (0·065 g.) of chlorine and dichlorodifluoromethane (Found: M, 100·1. Calc. for Cl_2: M, 71. Calc. for CCl_2F_2: M, 121) and a mixture (0·055 g.) of chlorotrifluoromethane and carbon tetrafluoride (Found: M, 98·5. Calc. for $CClF_3$: M, 104·5. Calc. for CF_4: M, 88). The reaction was quantitative, 97% of the carbon tetrachloride being accounted for in these volatile products. A much less volatile fraction consisting of a dark red liquid and a white solid had a molecular weight of 169 and contained vanadium, fluorine, and chlorine. Quantitative analyses confirmed the composition of the mixture as excess of pentafluoride (M, 146) and vanadium tetrachloride (M, 193). A very small amount of involatile yellow-green residue was shown to be vanadium trifluoride.

From 1·67 g. of carbon tetrabromide, after reaction at room temperature with excess of vanadium pentafluoride, 0·450 g. was recovered unchanged owing, presumably, to the formation of a protective coating of involatile vanadium salts. The remaining portion of the involatile residue dissolved readily in dilute alkali to give a green solution suggesting the presence of tervalent vanadium. Quantitative analyses showed the material to be a mixture of vanadium tribromide and tetrafluoride. The volatile products were carbon tetrafluoride (0·253 g.; Found: M, 92·5), bromotrifluoromethane (0·026 g.; Found: M, 158. Calc. for CF_3Br: M, 149), and an inseparable, dark red mixture of free bromine and excess of vanadium pentafluoride.

Carbon tetraiodide (1·74 g.), prepared by Walker's method,[8] was allowed to react for

[6] Fairbrother and Frith, *J.*, 1951, 3051.
[7] Haszeldine and Woolf, *Chem. and Ind.*, 1950, 544.
[8] Walker, *J.*, 1904, **85**, 1090.

48 hr. at room temperature with excess of vanadium pentafluoride. On fractionation, the volatile products were found to be carbon tetrafluoride (0·21 g.; Found: *M*, 92·5), trifluoroiodomethane (0·046 g.; Found: *M*, 198. Calc. for CF_3I: *M*, 195·9), and a mixture of iodine pentafluoride and excess of vanadium pentafluoride. This mixture was identified by molecular-weight measurements (Found: *M*, 164. Calc. for IF_5: *M*, 221·9. Calc. for VF_5: *M*, 146), and by both qualitative and quantitative analyses. Of the involatile black residue, only a small portion dissolved in water to give a blue solution, leaving a considerable amount of free iodine (approx. 1·0 g.). The aqueous solution contained iodide, fluoride, and vanadium in proportions corresponding to a mixture of vanadium iodide, VI_2, and vanadium tetra- and tri-fluorides.

Discussion

The melting point, 19·5° ± 0·5°, is in considerable disagreement with the results of Ruff and Lickfett [1] who reported that it does not melt in sealed glass tubes, even above 200°. However, they also reported its boiling point as 111·2°, and it seems highly probable that their samples of pentafluoride were badly contaminated with vanadium oxytrifluoride. The other pentafluorides of this sub-group of the Periodic Table, niobium and tantalum pentafluorides, have been shown to have m. p. of 80·0° and 91·5° respectively,[6] while a later value [9] for niobium pentafluoride is 78·9°. In a series of compounds such as the above three pentafluorides, higher m. p.s are to be expected with increasing molecular radii, so that this new value for vanadium pentafluoride is consistent and of the expected order.

The vapour-pressure measurements quoted above indicate that in the solid state, the vapour pressure obeys the relation $\log_{10} p(\text{mm.}) = 11{\cdot}049 - 2608/T$, while for liquid vanadium pentafluoride the corresponding equation is $\log_{10} p(\text{mm.}) = 10{\cdot}430 - 2423/T$. Hence the b. p. (extrapolated) is 48·3° ± 1° c, the latent heat of fusion 11,940 cal./mole, the latent heat of vaporisation 10,640 cal./mole, and the Trouton constant 33·1. Physically, the compound is thus very similar to molybdenum hexafluoride which melts at 17·5° and boils at 35°. The high value of the Trouton constant is of great interest, since it suggests considerable association in the liquid state. Iodine pentafluoride, for which the Trouton constant is 27·2, is said to associate and ionise as shown (eqn. 1), and in view of the isolation of stable hexafluorovanadates [2] containing the VF_6^- ion, it is reasonable to postulate that a similar process occurs in liquid vanadium pentafluoride (eqn. 2).

$$2IF_5 \rightleftharpoons IF_4^+ + IF_6^- \quad . \quad . \quad . \quad (1) \qquad 2VF_5 \rightleftharpoons VF_4^+ + VF_6^- \quad . \quad . \quad . \quad (2)$$

It is noteworthy that molybdenum hexafluoride with a normal value for the Trouton constant, 20·6, shows no signs of association, probably owing to the much greater instability of ions for which the central atom has co-ordination numbers of five and seven.

That the process (2) occurs in liquid vanadium pentafluoride is strongly supported by the conductivity measurements. The following values of the specific conductivities (ohm^{-1} $cm.^{-1}$; temperature shown in parentheses) also indicate that this ionisation occurs to a much greater extent than for iodine pentafluoride, or niobium and tantalum pentafluorides: TaF_5, $1{\cdot}56 \times 10^{-5}$ (95·1°) [10]; NbF_5, $1{\cdot}63 \times 10^{-5}$ (80·0°) [10]; IF_5, $2\text{—}3 \times 10^{-5}$ (25°) [11]; VF_5, $2{\cdot}4 \times 10^{-4}$ (25°) [12]; BrF_3, $8{\cdot}0 \times 10^{-3}$ (25°) [11]. If eqn. 2 is accepted, then the increase in conductivity on the addition of potassium fluoride is to be expected.

The fluorination with vanadium pentafluoride of the three carbon tetrahalides was undertaken to provide a means of determining the strength of the pentafluoride as a fluorinating agent, since similar reactions with bromine trifluoride and iodine pentafluoride had already been performed.[13] It was shown that, under conditions similar to

[9] Junkins, Farrar, Barber, and Bernhardt, *J. Amer. Chem. Soc.*, 1952, **74**, 3464.
[10] Fairbrother, Frith, and Woolf, *J.*, 1954, 1031.
[11] Banks, Emeléus, and Woolf, *J.*, 1949, 2861.
[12] Present work.
[13] Banks, Emeléus, Haszeldine, and Kerrigan, *J.*, 1948, 2188.

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those used here, the main products of the reactions of bromine trifluoride with carbon tetrachloride and with carbon tetrabromide were trichlorofluoromethane and bromotrifluoromethane respectively, while with carbon tetraiodide, dibromodifluoromethane and carbon tetrafluoride were produced. When it is remembered that the bromine in the reactant bromine trifluoride will considerably influence the products of the reactions, it is clear that vanadium pentafluoride appears to be just as effective as a fluorinating agent.

On the other hand, it was necessary to heat iodine pentafluoride and carbon tetrabromide to 90° to obtain an 83% yield of dibromodifluoromethane, while with carbon tetraiodide the main product was trifluoroiodomethane. Vanadium pentafluoride is therefore considerably more effective than iodine pentafluoride as a fluorinating agent, since not only does it react with carbon tetrabromide and tetraiodide at room temperatures to produce mainly carbon tetrafluoride, but in the latter case it also produces a certain amount of iodine pentafluoride.

Further work on vanadium pentafluoride is now in progress.

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407. *Studies in Polymorphism. Part VIII.* The Linear Rate of Transformation of β- into α-Sulphur at Low Temperatures and at Temperatures just below the Transition Point.*

By N. H. HARTSHORNE and M. THACKRAY.

Extension of the measurements of the linear rate to −15° has afforded further evidence that the activation energy for the transfer of molecules from the β- to the α-phase corresponds closely to the heat of sublimation of the former. At the lowest temperatures of the investigation the observed rate is about 10^3 times that calculated for a simple evaporation–condensation mechanism on the assumption that the rate of impact of molecules on the advancing α-surface is given by the Langmuir evaporation equation; but between 90° and the transition point (95·5°) the observed rate agrees with that calculated on this basis to within a power of 10.

Treatment of the results by Dunning's equation based on the theory of two-dimensional nucleation shows that above 80° the observed rate is far higher than that predicted from the application of the equation at lower temperatures.

IN Part VI [1] of this series, the linear rates of transformation of the enantiotropic monoclinic (β-)form of sulphur into rhombic (α-)sulphur over the range 0—80° were reported. With falling temperature the temperature coefficient of the rate appeared to tend towards a limiting value corresponding closely to the latent heat of sublimation of the β-form, suggesting that the activation energy of the transformation is the same as, or near to, that required for molecules to evaporate from the unstable form, or, in other words, that molecules in the transitional layer at the interface are energetically equivalent to molecules in the vapour state. This conclusion was in harmony with the results of an earlier study (Part III [2]), and if correct appeared to be of such fundamental importance for the theory of the transformation kinetics of molecular solids that it seemed desirable to test it further by extending the work to lower temperatures. New measurements, at

* Part VII, Hartshorne and Swift, *J.*, 1955, 3705.

[1] Hartshorne and Roberts, *J.*, 1951, 1097.

[2] Hartshorne, Walters, and Williams, *J.*, 1935, 1860.

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temperatures down to −15°, have therefore been made, with samples of sulphur purified by different methods, and these are described in the first part of this paper. The results accord well with the previous conclusion. The paper also reports measurements of the rate between 80° and the transition point, and these show a similar dependence of the rate on temperature to that found for carbon tetrabromide near its transition point (Part VII [3]).

Experimental

Purification of Sulphur.—Four specimens of sulphur, as follows, were used : (i) the residue of Specimen E used in the previous study (ref. 1, p. 1108); (ii) a similarly purified Specimen F (*i.e.*, recrystallised from carbon disulphide, and then melted and degassed), derived from the same batch of recrystallised sulphur as E; (iii) Specimen G, purified by the method of Bacon and Fanelli,[4] *i.e.*, by boiling it with magnesium oxide until a filtered sample gave no black spots on being boiled for a few minutes in a clean dust-free Pyrex test-tube, the starting material being B.D.H. " crystalline " sulphur as used for E and F; (iv) Specimen H, supplied by the British Rubber Producers' Research Association by the kindness of its then Director, Dr. G. Gee, F.R.S., and purified by Bacon and Fanelli's method and then vacuum-distilled, the starting material being flowers of sulphur. Before use, Specimens G and H were annealed at 100° for 2 days in order to convert the insoluble sulphur (resulting from the heating of the liquid to the boiling point in the purification process) into the soluble form. The amount of this insoluble sulphur, determined by extraction with carbon disulphide, was 2—3%.

Bacon and Fanelli's method removes traces of organic impurity, which, according to these authors, the more conventional methods fail to do. The presence of such impurity is shown by the black-spot test (above), which they claim is sensitive to 1 part per million. The recrystallised sulphur from which Specimens E and F were prepared gave a slight black spot reaction.

The source material from which E, F, and G were prepared gave a negative reaction for selenium when tested by Hughes and Wilson's method.[5] Mr. C. H. Manley, the City Analyst of Leeds, very kindly tested F, G, and H for the presence of arsenic, using the method given in the British Pharmacopœia, 1948, and found : in F, 0·0004%; in G, 0·0002%; in H, nil. Insufficient of E was left for any to be spared for this test, but it is unlikely that it would have differed appreciably from F. Specimen G was also tested for the presence of sulphur dioxide and hydrogen sulphide by allowing a finely ground sample to remain in contact with dilute permanganate solution for two days, but no decolorisation was observed. (These gases would be formed in the Bacon–Fanelli process as results, respectively, of the long period of boiling and the destruction of hydrocarbon impurity, and some might have been retained in the solid sulphur.)

The absorption spectra of alcoholic solutions of F, G, and H showed no differences in either the visible or the ultraviolet region. The arc spectra of these specimens, obtained with pure carbon electrodes and a copper spark for calibration, showed only the occasional presence of silicon as an impurity, and this might have been due to small particles of glass which were liable to be present in all specimens, since in all cases the final stage in the purification leaves the sulphur as an intractable block in a glass tube from which it is extracted by gently breaking up the glass in a mortar (see, *e.g.*, Part V,[6] p. 589).

The m. p.s of the specimens were compared in pairs on a hot stage under the microscope, the temperature being raised very slowly. No differences were detected, other than that due to some particles' escaping transformation after passing the transition point and melting as α-sulphur.

From the above tests and observations it may be concluded that all the specimens were chemically pure by ordinary standards.

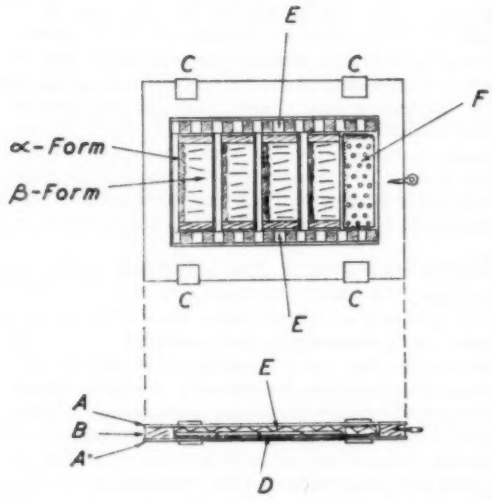
Preparation of Slides.—As in earlier work on sulphur in this series, the transformation was studied in polycrystalline films confined in glass–mica–glass cells (these with their sulphur films being referred to in the sequel simply as " slides "), and mostly covering the same range of thicknesses (0·06—0·10 mm.). In the hope of reducing the variance in the rate between slides,

[3] Hartshorne and Swift, *J.*, 1955, 3705.
[4] Bacon and Fanelli, *Ind. Eng. Chem.*, 1942, **34**, 1043.
[5] Hughes and Wilson, *J. Soc. Chem. Ind.*, 1936, **55**, 359.
[6] Elias, Hartshorne, and James, *J.*, 1940, 588.

the temperature at which the β-form was crystallised was controlled more closely than before by adopting the following procedure. The hot plate, made of aluminium, was recessed on top to take the slide, and the recess was normally covered with a thin glass plate to protect the slide from draughts. When the sulphur was completely melted (at a temperature not exceeding 123° as before), the apparatus was allowed to cool until the temperature reached 108° ± 1°, and the β-form was then caused to crystallise by running a platinum point along the edge of the film. This temperature was chosen as giving most nearly the same texture of β-film as did the previous method (ref. 6, p. 589). Since the slide was protected during cooling by the glass plate, and the cooling was quite slow, about 6 min. being usually required before the temperature reached 108°, it is probable that the temperature of the slide closely followed that of the plate.

The slides used in some runs at the lower temperatures were annealed by heating them in a closed vessel at 100° for two days after the β-form had been brought out from the melt, in order to convert into soluble sulphur, the small amount of the insoluble form (about 0·1% as determined on separate samples by extraction as before) resulting from the melting of the sulphur in preparing the films, and, for Specimens E and F, in the final stage of the purification. A statistical comparison between the rates given by annealed and unannealed slides made with the same specimen showed, however, no significant difference.

FIG. 1.



Methods of Measuring the Interface Advance.—In the low-temperature work, measurements were made at −15° and 0°. For work at −15° a cold room with thermostatic control to ±0·1° was used, and the 0° thermostat was a large, well-lagged, Dewar vessel containing melting ice, and stationed between the double doors leading to the cold room. The top of the Dewar vessel was closed with a thick cork cover, and the slide boxes (see below) were placed in a central container made of copper sheet.

After being inoculated the slides were placed in groups of four in flat transparent boxes (Fig. 1), built up from two sheets of thin glass *A*, held against a Perspex frame *B* by four strong phosphor-bronze clips *C*. The Perspex–glass junctions were sealed with silicone vacuum grease. The four slides, which were of the type used at 0° in the earlier work (ref. 1, p. 1099), were supported film downwards with their two free ends resting on brass strips *D*, and were held in that position by crimped strips of copper foil *E* as shown. Calcium chloride in a perforated zinc container *F* maintained a dry atmosphere in the box.

While in the cold room at −15°, these boxes were kept under a cover made of thick corrugated cardboard to prevent their being affected by any temporary rise of temperature which might occur when the room was entered. Observations of a thermometer fixed in the cardboard cover showed no appreciable change in its inside temperature on these occasions, which in any case were infrequent.

Records of the position of the interface were made by laying the box with the sulphur films downwards on a photographic plate, and exposing it to the light from a 48-w compact-filament microscope lamp, masked by a stop of *ca.* 3/16 in. diameter, and fixed a few feet above the cell. This was done in the cold room, which was illuminated by a red safe-light during the operation. Calculations showed that under these conditions the lamp should behave effectively as a point source and that the image, or rather shadowgraph, of the films cast on the plate would not be appreciably magnified. In fact extremely sharp records were obtained, which showed the position of the interface with great clarity. Ilford Ortho Halftone plates developed for maximum contrast were used. Measurements of the rate of advance of the interface were

made by projecting the negatives in sequence on to a gridded screen as in the earlier work at 0° (ref. 1, p. 1100).

In order to extend the range over which comparison with previous work could be made, the boxes were placed in a constant-temperature room at 22° ± 0·5° after the runs at −15° and 0° were finished, and the films photographed at the beginning and end of a known interval of time by the method described above. The measurements obtained from these records were of a lower order of accuracy than the rest, since by this time the contour of the interface had usually become very ragged, and because of the rather poor temperature-control, but they served as a check on the behaviour of the different specimens in this temperature region.

For work at temperatures near the transition point (T_0), the projection apparatus of Hartshorne and Roberts [1] was used, the slides being studied singly. Since in general only two records of the position of the interface were now required at each temperature (see below), the tedious and exacting method of following the advance visually was abandoned and the following substituted. A grid very similar to that used on the screen in the visual method, but corresponding to a much smaller magnification (× 11·4) was scribed on a sheet of Perspex by means of a milling machine, and the lines well blacked by rubbing with Indian ink. This Perspex sheet was hinged vertically to the adjustable screen of the projection apparatus, and could be folded flat against it and held in that position by a catch. The distance between the projector and the screen having been adjusted to give the same magnification as that of the grid, and the screen adjusted to make the image of the film edge coincident with the zero vertical line on the grid, the room was darkened except for a red safe-light, a strip of bromide paper was placed between the grid and the screen, and the catch secured. By switching on the projector lamp (exposure 2—3 sec.) a record of the film showing the position of the interface superimposed on the grid was obtained. From a series of such records, the advance of the interface in each section of the grid could be quickly read off.

The type of inoculating brush used in the earlier work would not withstand the higher temperature of 90° to which the work was now extended, and a fine steel point was used instead. Although the action of this was purely mechanical, it was almost invariably effective in initiating transformation along the whole of the edge of the film in this temperature region.

Results

At Low Temperatures.—An analysis of the variance of some of the results obtained previously [1] showed that the groups of measurements obtained on individual slides, *i.e.*, the " Δ values " (times to advance over small sections of the films), cannot be regarded as random samples of the whole population of measurements (cf. results with carbon tetrabromide [3]). Thus at 10° the ratio of the variance between slides to that within slides was 40, whilst the corresponding ratio at 0° was 23. For a probability of 5% and the very large number of degrees of freedom within slides (228 and 1148 respectively), these values correspond to a very highly significant difference between the slide mean rates, which must therefore be regarded as the individual measurements from the standpoint of statistical analysis. The meaning of this is of course that despite the care taken to prepare the films under closely similar conditions, not all the factors determining the mean rate of advance of the interface in a slide are in fact under complete control. Included among these factors may be variations in the orientations of the β-crystals and in their secondary structure, and in the distribution of dislocations or other growth-assisting imperfections in the α-phase.

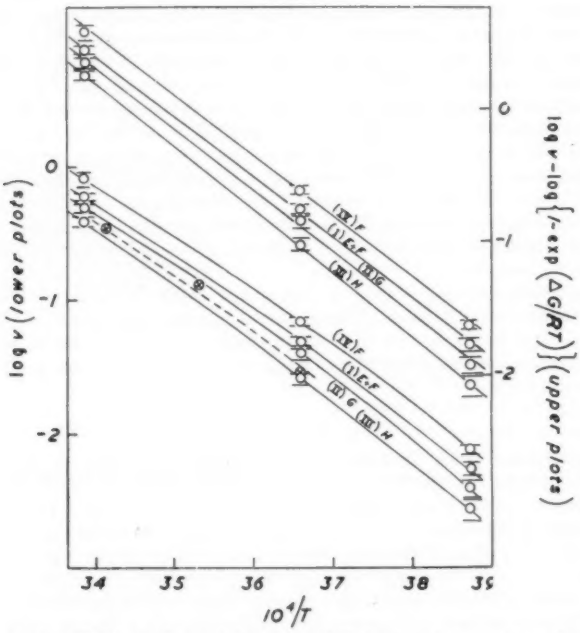
In view of this, and of the constancy of the rate which had been found at the lower temperatures (see, *e.g.*, ref. 1, plots for 0° and 20° in Fig. 3) and was confirmed at −15° by a preliminary experiment in the present work, there seemed to be no point in continuing with the earlier method of making a large number of measurements at successive short distances of advance. At each temperature therefore only two positions of the interface were now recorded to obtain the slide mean rate.

In another analysis of the previous results, plots of log v against $1/T$ were found to give practically the same slopes at corresponding temperatures, irrespectively of whether v was based on the upper 10% of the Δ values, or on the lower 10%, or on all these values. This showed that the variance in the rate was due mainly, if not wholly, to variance in the non-exponential factors determining the rate, and not much, if at all, to variance in the activation energy. In the present work, a " split-run " procedure was followed, measurements being

made at −15°, 0°, and 22° on every slide studied (half the slides being done at −15° first, and half at 0° first), with the object of keeping the non-exponential factors constant as far as possible, and this procedure yielded values of the logarithm of the temperature coefficient lying within narrow limits of probability, as will appear below.

Fig. 2 shows the plots (lower group of curves) of the logarithms of the mean slide mean rates against $10^4/T$ for different sets of slides. 95% fiducial limits are indicated by short strokes above and below each point. The three lower full-line curves are for sets differing in respect of the source and method of purification of the sulphur used, thus : set (I) 17 slides prepared with Specimens E and F (3 with E, 14 with F) ; set (II) 12 slides prepared with Specimen G ; set (III) 14 slides prepared with Specimen H. In all these slides the film thicknesses were within the range 0·6—0·10 mm. as in the earlier work. The differences in rate shown by these 3 sets are

FIG. 2.



The uppermost plots (IV) *in each group have been shifted upwards to avoid overlap with* (I).
⊗ Earlier results.
Plots (IV) are for thicker films.

significant, and the rates for set (I) are 50—100% greater than those for set (III). The uppermost curve in the group, (IV), is for a set of 7 slides prepared with Specimen F, which had films 0·11—0·15 mm. thick. These gave mean rates 10—20% greater than the thinner ones prepared with this specimen, in qualitative agreement with earlier observations of the effect of film thickness (ref. 6, p. 595). In plotting this last curve the vertical scale has been shifted upwards a little in order to avoid overlap with the point circles of set (I). The group also contains the smoothed curve (broken line) * drawn through the earlier results [1, 6] obtained at 0°, 10°, and 20°. It will be noted that there are no marked differences in the slopes of these five curves.

The upper plots in Fig. 2 show the result of applying Hartshorne's equation, *i.e.*, the linear law (see ref. 3, p. 3717), to the new results, by plotting $\log v - \log\{1 - \exp[q(1/T_0 - 1/T)/\boldsymbol{R}]\} = \log v - \log\{1 - \exp(\Delta G/\boldsymbol{R}T)\}$ against $10^4/T$, ΔG, the free-energy increase attending the reverse

* Lest this smoothing should appear rather arbitrary in the present figure, it should be explained that it depends also on the points obtained for higher temperatures (see, *e.g.*, Fig. 1, ref. 9).

transformation, being calculated from Lewis and Randall's equation.[7] [Values of ΔG based on more recent heat-capacity data (Eastman and McGavock [8]) are nearly the same, and do not affect the plots appreciably.] This should give a straight line if the equation is obeyed, and it is evident that this condition is nearly fulfilled, in fact straight lines are drawn in the Figure and these lie inside the 95% limits in all cases. Since, however, the earlier results indicated a closer conformity with the equation the lower the temperature (Hartshorne [9]), and the results at 22° are less trustworthy than the others, as explained above, we have used only the results at 0° and −15° to estimate the activation energy. Between these two temperatures there was no significant difference between the temperature coefficients for set (II) (G) and set (III) (H), so a mean value for these two sets has been calculated. This is a little, but significantly, higher than the mean value for sets (I) (E + F) and (IV) (F, thicker films) which gave almost identical coefficients. The split-run procedure led to a high degree of correlation between v_0 and v_{-15} for these two main groups of slides, the correlation coefficients (by ranks) being 0·83 for the former group (G + H), and 0·82 for the latter (E + F). The activation energies and their 95% limits corresponding to these results are 23·1 ± 0·6 kcal./mole for G and H, *i.e.*, those specimens purified by the Bacon and Fanelli process, and 21·9 ± 0·4 kcal./mole for E and F, *i.e.*, those specimens purified by recrystallisation and degassing. These values accord well with 22·6 kcal./mole, the mean internal latent heat of sublimation of β-sulphur between T_0 and −15° derived from the vapour-pressure data of Neumann [10] and Bradley [11] (which are very closely consistent), and Lewis and Randall's equation for the heat of transformation,[7] and support our previous conclusion regarding the activation energy.

From the differences between the rates of the different " pure " specimens (Fig. 2), it is clear that the rather good degree of reproducibility obtained in the earlier work [6, 1] cannot be depended on when the range of specimens and methods of purification are extended. The differences are probably due to varying minute amounts of impurities (possibly also to physical contamination by broken S_8 rings in some cases), and it is perhaps not surprising that these should have a significant effect on the rate. We may distinguish two possibilities : (i) that the impurities affect the secondary structure of the β-phase and that this influences the rate (see later); (ii) that in the case of impurities which have a solvent action on sulphur, they may reduce the activation energy by establishing a solution layer in place of a vapour layer at the interface, though perhaps only locally.

The reproducibility of the temperature coefficient, particularly for groups of slides in which the same or similarly purified specimens of sulphur were used, may be regarded as very good, and this is much more important than a close reproducibility of the rate. Thus set (I) may be broken down into three groups as follows : (*a*) 3 unannealed slides prepared with Specimen E; (*b*) 6 unannealed slides prepared with Specimen F; (*c*) 8 annealed slides prepared with Specimen F. These three groups together with set (IV) (F, thicker films) gave temperature coefficients between 0° and −15° the logarithms of which agreed to within just over 1%. The logarithms of the temperature coefficients for sets (II) and (III) (G and H) agreed to within just over 3%.

The reason for the somewhat lower temperature coefficient given by E and F, than by G and H, may be that the method of purification used for the former specimens did not completely remove all solvent impurities, *e.g.*, the carbon disulphide used in the recrystallisation.

At Temperatures near the Transition Point (T_0).—Measurements were made at 80°, 85°, and 90° on each slide. Specimens G and H were used since the chemical tests and the low-temperature measurements had indicated that they were likely to be the purest.

In the previous work, the rate at the higher temperatures was not strictly constant over the range 0—2 mm., but showed a rather marked initial increase (ref. 1, Table I). A detailed analysis of the results obtained at 60°, 70°, and 80° in this work has shown that for the large majority of slides the rate became sensibly constant after an initial advance of 0·5—1·0 mm., provided that the slide had then been in the thermostat for at least 80—90 min., *i.e.*, that both a distance effect and a time, or annealing, effect were involved.

The result of this analysis formed the basis of the method of starting an experiment in the

[7] Lewis and Randall, *J. Amer. Chem. Soc.*, 1914, **36**, 2468.
[8] Eastman and McGavock, *J. Amer. Chem. Soc.*, 1937, **59**, 145.
[9] Hartshorne, *Discuss. Faraday Soc.*, 1949, **5**, 149.
[10] Neumann, *Z. phys. Chem.*, 1934, **171**, 416.
[11] Bradley, *Proc. Roy. Soc.*, 1951, *A*, **205**, 553.

present work. After the slide had been in the thermostat for about 30 min., it was inoculated and the interface allowed to advance to an estimated mean distance of 0·75 mm. from the film edge. The first photographic record was then made. This stage should have been reached about 80 min. after the slide was inserted in the thermostat if the initial rate had been the same as in the earlier work, but most of the present slides proved to have greater rates than this, and measurements on them were in fact started before the full annealing time had elapsed. However, a statistical comparison between the mean rates for these slides and for those fully annealed showed a difference, in the expected direction to be sure, but of only doubtful significance. (This only concerns measurements at 80°. By the time that measurements at 85° and 90° were made, the full annealing time had been exceeded in all cases.)

On the majority of the 11 slides studied (4 made with Specimen G and 7 with H), the interface advanced in a comparatively regular manner over all its length, but in a few slides one or two promontories developed, usually in the later stages of the experiment, which could fairly be described as representing an " abnormal " rate of advance (ref. 1, p. 1108). The advance of these promontories was not included in the measurements on which the slide means were based. (Abnormality in this temperature range in the earlier work was associated with those specimens which melted as α-sulphur. Observations on powdered G and H on the microscope hot stage showed that a considerable proportion of the particles melted as α-sulphur.)

There was no significant difference between the mean rates shown by the two specimens at any of the higher temperatures, and their results have therefore been pooled. This contrasts with what was found at low temperatures (see Fig. 2), and may have been partly due to the greater variance in the rates (95% limits ranging from ±21—44%, in contrast to ±8—19% at low temperatures). This in turn may have been partly due to the smaller number of slides of each specimen studied, though an increase in the variance near T_0 is to be expected, since quite small changes in the conditions at the interface, such as local temperature fluctuations, will have a relatively large effect on the supersaturation.

The results are plotted in Fig. 3 (curve A), the 95% limits being indicated as in Fig. 2. The curve is asymptotic to the temperature axis as was found for carbon tetrabromide.[3] The rates (in mm./hr.) and 95% limits are: 80°, 2·58 ± 0·54; 85°, 0·72 ± 0·18; 90°, 0·131 ± 0·057. The value at 80° is higher than the figure of 1·62 ± 0·14 obtained by Hartshorne and Roberts [1] at this temperature with " normal " sulphur purified by recrystallisation and degassing. (This figure refers to the advance beyond 0·75 mm. from the film edge, so that it can be compared directly with the present results. The figure 1·60 previously published was the mean rate of advance beyond 0·25 mm. from the film edge.) This discrepancy can, however, be reasonably attributed to the fact that G and H showed a slightly higher temperature coefficient, *i.e.*, a steeper mean-rate curve, at lower temperatures than the specimens purified by recrystallisation and degassing, as were all the earlier ones. They might therefore be expected to show a higher rate than the latter specimens at higher temperatures.

In any case it seems justifiable to take the present results at 80°, 85°, and 90° as consistent among themselves since the split-run procedure was followed. There was in fact a high degree of correlation between v_{85} and v_{90}, namely, 0·74 (by ranks), though no significant correlation between v_{80} and v_{90}.

Discussion

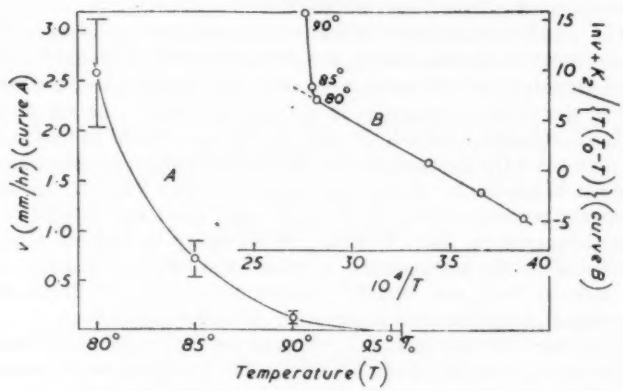
It has been shown in earlier papers [9, 1] that the rate in the lower temperature range is considerably greater than that calculated from the linear law, assuming a simple evaporation–condensation mechanism. The value of the factor (B) by which the observed and calculated rates differ, depends on the expression used for the rate of evaporation of molecules from the β-phase, which will be equal to the rate of impact of molecules on the growing α-phase for an interface region of the order of one or a few molecular diameters in thickness (see ref. 3, p. 3717). If this rate be expressed (in terms of molecules per lattice site) as $\nu \exp(-L_{II}/\boldsymbol{R}T)$, where ν is the vibration frequency of the surface molecules, taken as 10^{12}—10^{13}, and L_{II} is the internal latent heat of sublimation of β-sulphur, B works out to $\sim 10^7$ (see ref. 9, p. 156 *). Now:

$$\nu \exp(-L_{II}/\boldsymbol{R}T) = (p_{II}/p_I)\, \nu \exp(-L_I/\boldsymbol{R}T) = (x+1)\, \nu \exp(-L_I/\boldsymbol{R}T)$$

* In the calculation referred to here a modified form of the linear law equation was actually used, but this makes no difference to the order of the value of B.

where p_{II}, p_I are the vapour pressures of β- and α-sulphur respectively, x is the supersaturation, and L_I is the internal latent heat of sublimation of the α-sulphur. In this treatment, $\nu \exp(-L_I/RT)$ expresses the rate of impact of molecules on α-sulphur from the vapour at its equilibrium pressure, and this will be equal to the rate of evaporation of α-sulphur if the condensation coefficient is unity. Since, however, Bradley [11] found that the actual rate of evaporation is $\sim 10^4$ times that given by this expression, but that it agrees with that given by the Langmuir evaporation equation with a condensation coefficient of approximately unity, it seems clear that a more realistic calculation of the rate of transformation to be expected for a simple evaporation–condensation mechanism will be made if the Langmuir equation is substituted for the expression given above. This follows a similar procedure suggested by Bradley in the work on carbon tetrabromide (see ref. 3, p. 3720.) Starting with the convenient form of the linear law given by the dislocation theory of crystal growth from the vapour, namely, $v = \nu d \exp(-L_I/RT)\, x$, where v is the linear rate, and d the mean lattice spacing, and substituting for $\nu \exp(-L_I/RT)$ the expression $Nd^2p_I/(2\pi MRT)^{\frac{1}{2}}$,

FIG. 3.



the rate of impact of molecules on α-sulphur from the equilibrium vapour as given by the Langmuir equation (N is the Avogadro number) we obtain for the linear rate

$$v = Nd^2p_Ix/(2\pi MRT)^{\frac{1}{2}} \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad \text{(i)}$$

By taking the pooled results for Specimens G and H, and calculating p_1 from Bradley's [11] and Neumann's [10] data, and x from the expression $[\exp(-\Delta G/RT) - 1]$, this equation gives B = constant at $2{\cdot}1 \times 10^3$ at −15° and 0°, falling to $1{\cdot}5 \times 10^3$ at 22°, followed by a more rapid fall to *ca.* 10^2 at 80°, and $3{\cdot}6$ at 90°. Interpolation of curve *A*, Fig. 3, between 90° and T_0, which can be done with rather good reproducibility up to 94° by using a steel-strip curve-tracer, shows that the further application of eqn. (i) gives $B = 1$ at *ca.* 94°. This interpolation, however, suggests another interpretation of the results near T_0, since between 90° and 94° the interpolated values are very nearly proportional to the square of the supersaturation, *i.e.*, they obey approximately the parabolic law in dislocation theory, as was found in the case of carbon tetrabromide.[3] This would be consistent with the asymptotic approach of the rate curve to T_0, which on the above interpretation in terms of eqn. (i) arises from the progressive decrease in B as T_0 is approached. (The unmodified linear law requires that dv/dT is finite at T_0.)

The equation for the parabolic law put into the same form as eqn. (i) would be :

$$v = Nd^2p_I(x^2/x_I)/(2\pi MRT)^{\frac{1}{2}} \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad \text{(ii)}$$

where x_{I_1} the critical supersaturation, is given by $(2\pi\gamma_M/RT)\exp\{-(W_s' - U_s)/2RT\}$, where γ_M is the edge free energy of the growth step per mole, W_s' is the molar evaporation energy of surface-adsorbed molecules, and U_s is the molar activation energy for such molecules to migrate from one lattice site to an adjoining one (Burton *et al.*[12]). It is possible to set a lower limit to x_I, since it cannot be less than the value of x at 90°, namely, 0·018, if the square law holds down to this temperature. The upper limit is determined by (*a*) the maximum value assumed for γ_M, and (*b*) the minimum value assumed for $(W_s' - U_s)$. We have based (*a*) on a surface free energy of 100 ergs cm.$^{-2}$, *i.e.*, a value somewhat greater than that (60 ergs cm.$^{-2}$) of the liquid just above the melting point, and for (*b*), following Burton *et al.*,[12] we have taken a value somewhat less than $L_I/2$, namely, 11,000 cals. These considerations lead to $x_I = 0{\cdot}0189$ at 91° and 0·0201 at 94°, and applying eqn. (ii) we obtain $B = ca.\ 3{\cdot}6$ at 91° and *ca.* 3·1 at 94°.

Thus, whichever interpretation is correct, the rates near T_0 agree with those predicted for a simple evaporation–condensation mechanism to within a power of 10, provided that the Langmuir evaporation equation applies (as it is known to do for the evaporation of α-sulphur into a free vapour space), and that the critical supersaturation has not been grossly underestimated (which seems unlikely).

It should be noted that although for convenience we have made use of the equations of the dislocation theory of crystal growth, the above conclusions would be equally valid for any system of perpetual growth steps, no matter how perpetuated, if their spacing apart were related to the supersaturation as in dislocation theory. As far as the application of the linear law is concerned indeed, the only requirement would be that the spacing of the steps be less than twice the mean migration distance of surface adsorbed molecules.

The " mosaic block-crack " theory put forward in Part VI (ref. 1, p. 1113) to account for the discrepancy represented by the B factor does not seem capable of explaining its decrease with temperature, since it would be necessary to suppose that the block size decreases with rise in the temperature at which the rate is measured, whereas it is to be expected that the block size would be determined by the conditions under which the slides were prepared, and these conditions were the same throughout.

Cagle and Eyring [13] have proposed an equation for the rate of phase transformations in solids, which is based on transition state theory. Their paper is mainly concerned with the transformation between white and grey tin, which certainly does not proceed by way of an intermediate vapour-type phase, but mention is made of the sulphur transformation, including a reference to the earlier work in this series (Part V),[6] though not to the later work.[1] The equation is not applied in detail to this case because of lack of data, but the transformation is evidently regarded as amenable to this treatment in principle. It does not seem to us, however, that this approach can clarify the problem of the B factor, if, as we believe, the primary step in the transformation process involves the formation of an intermediate phase in which the molecules are energetically equivalent to molecules in the vapour state. Transition-state theory would interpret the existence of the B factor as due to an increased entropy of activation, and it is difficult to see how the transition state could possess greater disorder than if it were a vapour. This and other theories of solid–solid reaction kinetics have been recently discussed more fully by Bradley.[14]

We therefore seem to be forced back to the idea of a secondary step of low activation energy in the transformation process to account for the high rates (as was visualised in the mosaic block-crack theory), though as shown above it does not seem possible to relate this directly to mosaic-block dimensions. It is possible, however, that the secondary structure of the crystals enters into this mechanism in some way. A detailed study of the advance of the interface by high-power microscopy, which is now in progress, may possibly throw some light on this problem.

[12] Burton, Cabrera, and Frank, *Phil. Trans.*, 1950—51, **243**, *A*, 299.
[13] Cagle and Eyring, *J. Phys. Chem.*, 1953, **57**, 942.
[14] Bradley, *ibid.*, 1956, **60**, 1347.

Fig. 3, curve *B*, shows the application of Dunning's equation (ref. 9, p. 156) to the pooled results obtained with Specimens G and H, it being assumed for the purpose of calculating the second constant, that the equation is valid up to 80°. {The equation, $\ln v = \ln K_1 - E/\boldsymbol{R}T - K_2/[T(T_0 - T)]$, is applied by first plotting $\ln v + E/\boldsymbol{R}T$ against $1/[T(T_0 - T)]$, using an assumed value for E. From the slope of this plot, which should be a straight line if the correct value of E has been selected, K_2 is obtained. The plot of $\ln v + K_2/[T(T_0 - T)]$ against $1/T$ then gives a value for E. If this does not agree with that previously assumed, the value which fits both plots is determined by a process of successive approximation.} The four lower points, corresponding to the range −15° to 80°, lie on quite a good straight line with a slope equivalent to an activation energy of 22·6 kcal./mole, but the results at 85° and 90° show a strong positive deviation from the requirements of the equation, as did those obtained with carbon tetrabromide near its transition point.[3] The result of applying the equation is striking, but the difficulties associated with this theory[9,1] do not seem to lose their importance after further consideration—namely the very low value of the edge free energy implied by the value of K_2, and the improbability that two-dimensional nucleation would be a necessary condition for sustained growth on such an obviously imperfect surface as is presented by the advancing front of the rhombic phase in the lower temperature range. The new finding that the observed rate above 80° deviates radically from the requirements of the equation is, however, of interest.

One of us (N. H. H.) thanks the Council of the Chemical Society for a Research Grant. We are greatly indebted to Dr. B. L. Welch for assistance with the statistics of this problem, and to Dr. R. S. Bradley with whom we have had many helpful discussions during the course of the work.

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408. *The Conductivity of Some Quaternary Ammonium and Amine Picrates in Acetonitrile at 25°.*

By C. M. French and D. F. Muggleton.

The conductivity, in acetonitrile at 25°, of three tetra-*n*-alkylammonium and two amine picrates has been investigated in the concentration range $4{\cdot}77 \times 10^{-6}$ to $6{\cdot}25 \times 10^{-3}$N, and the limiting equivalent conductance Λ_0 computed for each salt. In $<10^{-3}$N-solutions, tetraethyl-, tetra-*n*-butyl-, and tetra-*n*-pentyl-ammonium picrate conformed to the Debye–Hückel–Onsager equation, the plots of Λ against $c^{0.5}$ being linear. For $>10^{-3}$N-solutions the plots become convex to the concentration axis. Aniline picrate dissociates simultaneously into ionic and molecular species, and the magnitudes of the respective dissociation constants indicate that the non-ionic process predominates. Tribenzylamine picrate, however, appears to exist in acetonitrile almost exclusively in an ionic form, in contrast to its behaviour in other solvents. Dissymmetry in the cation markedly reduces the dissociation constant. The effect of the solvent on these several equilibria cannot adequately be expressed solely in terms of the macroscopic dielectric constant.

The present theory of conductivity is based, in part, on the assumptions that the solvent medium is continuous and isotropic, and that its influence on ionic processes can be described in terms of a macroscopic dielectric constant and macroscopic viscosity. It has been pointed out, however, that if the solvent is composed of large molecules the above assumptions can no longer be justified and anomalous effects may arise.[1] In work, to be

[1] Fuoss and Elliott, *J. Amer. Chem. Soc.*, 1939, **61**, 294.

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reported later, on the conductance of certain tetra-*n*-alkylammonium and amine picrates in non-aqueous media having large molecules, it was deemed necessary to use an additional solvent as a reference standard with which to compare the conductance–concentration relations of these systems. Acetonitrile was chosen since its molecule is very small, and the solvent may here be presumed to approximate to the ideal isotropic continuum; further, its dielectric constant is high enough for direct extrapolation of experimental data so as to provide reasonably accurate values for the limiting conductances of the various salts. The behaviour of these electrolytes in acetonitrile is broadly in agreement with current theory and with other published results. Certain points, however, require comment since there is some evidence of solvent effects which cannot adequately be explained in terms of the present theory.

Experimental

Conductance was measured by the method, and with the equipment, described earlier [2] for the more highly conducting dialkyl phthalate solutions.

The dielectric constant of acetonitrile was measured on a low-voltage Schering bridge in a cell previously calibrated with air and benzene.

Solvent viscosity was determined in an Ostwald viscometer of standard pattern.

Materials were prepared and purified as follows: acetonitrile was allowed to stand over solid potassium hydroxide, then over calcium chloride, refluxed over phosphoric oxide for 50 hr., and repeatedly distilled from fresh portions of this oxide. It was not possible to reproduce Walden and Birr's observation [3] that the phosphoric oxide eventually remained colourless: our experience is similar to that of Smith and Witten.[4] The solvent was fractionated from anhydrous potassium carbonate through a 75 cm. column packed with Fenske helices, first and last fractions (each 10% of the whole) being rejected. The purified material was twice redistilled, only the middle fraction being collected. At all stages the solvent was protected with phosphoric oxide from atmospheric contamination. Our product had b. p. 81·7°/760 mm., n_D^{20} 1·3438, d_4^{25} 0·7767, ε_{25} 36·2, η_{25} 0·34376 centipoise, κ_{25} $5{\cdot}41 \times 10^{-8}$ mho (lit., b. p. 81·7°/760 mm.,[4] n_D^{20} 1·3438,[5] d^{25} 0·7767,[4] 0·77683,[3] η_{25} 0·3437$_6$,[3] κ_{25} $5{\cdot}39$—$8{\cdot}60 \times 10^{-8}$ mho[3]).

Tetraethylammonium picrate was prepared in two ways from recrystallised tetraethylammonium bromide: (*a*) This salt was shaken with an aqueous suspension of freshly prepared silver oxide at 45°, the whole then filtered through sintered glass and neutralised with the calculated quantity of picric acid; the product was recrystallised several times from conductivity water. (*b*) The bromide was treated with silver picrate in alcohol. The organic picrate was twice precipitated from hot alcohol by addition of water and of ethyl acetate severally. The two products dried at 110° and stored in a vacuum desiccator over phosphoric oxide had identical physical properties, *viz.*, m. p. 255·8° (lit., m. p. 255·5—255·8°,[6] 255·8°,[7] 256° [8]).

Tetra-*n*-butyl- and tetra-*n*-pentyl-ammonium picrate were obtained by metathesis of silver picrate in hot alcoholic solution with the corresponding quaternary ammonium bromide which had been prepared by Ostwald and Roederer's method.[9] In each case the tetra-alkylammonium picrate was repeatedly crystallised from alcohol, the final product being dried for some weeks *in vacuo* over phosphoric oxide. Tetra-*n*-butylammonium picrate had m. p. 89·5° (lit., m. p. 89°,[3] 89·5° [10]). Tetra-*n*-pentylammonium picrate had m. p. 74° (lit., m. p. 73°,[11] 73—74° [6]).

Aniline picrate was prepared by mixing hot alcoholic solutions of freshly distilled aniline and picric acid. The solution was evaporated until crystallisation commenced, and was then

[2] French and Singer, *J.*, 1956, 1424.
[3] Walden and Birr, *Z. phys. Chem.*, 1929, **144**, 269.
[4] Smith and Witten, *Trans. Faraday Soc.*, 1951, **47**, 1304.
[5] Partington and Cowley, *Nature*, 1935, **135**, 474.
[6] Tucker and Kraus, *J. Amer. Chem. Soc.*, 1947, **69**, 454.
[7] Walden, Ulich, and Laun, *Z. phys. Chem.*, 1924, **114**, 275.
[8] *Idem, ibid.*, 1923, **106**, 49.
[9] Ostwald and Roederer, *Kolloid Z.*, 1938, **82**, 174.
[10] Mead, Fuoss, and Kraus, *Trans. Faraday Soc.*, 1936, **32**, 594.
[11] Vernon and Masterson, *J. Amer. Chem. Soc.*, 1942, **64**, 2822.

rapidly chilled in ice. The product, purified by recrystallisation from alcohol and dried *in vacuo* over phosphoric oxide, had m. p. 178—179° (decomp.) [lit., m. p. 175—177° (decomp.) [1]].

Tribenzylamine picrate was obtained by interaction of the base with a slight excess of picric acid in hot alcohol. The precipitated salt was recrystallised several times from 7 : 3 ethyl alcohol–acetone and dried at 100° before storage *in vacuo* over phosphoric oxide. The product had m. p. 191° (lit., m. p. 191° [1]).

" AnalaR " benzoic acid, recrystallised several times from hot conductivity water, dried by prolonged storage over phosphoric oxide, and sublimed at about 110°, had m. p. 121·7° (lit., m. p. 121·7° [12]).

Conductivity water was prepared from the laboratory supply of distilled water in a Bousfield still equipped with a block-tin condenser. It had κ_{25} 1×10^{-6} mho.

Results.—The variation in equivalent conductance with concentration for all the systems is recorded in Table 1. A solvent correction applied to the experimental readings consisted simply of subtracting the solvent conductance from that of the solution.

TABLE 1. *Conductances of the picrates in acetonitrile at 25°.*

Et_4NX		Bu_4NX		$(C_5H_{11})_4NX$		$(CH_2Ph)_3NHX$		$Ph{\cdot}NH_3X$	
10^4c	Λ	10^4c	Λ	10^4c	Λ	10^4c	Λ	10^4c	Λ
36·927	142·63	45·760	118·84	38·953	111·81	60·476	87·343	62·530	46·742
27·683	144·92	21·355	123·89	24·605	115·21	40·159	93·651	38·951	51·087
17·795	148·71	16·608	126·18	16·755	118·72	29·880	98·332	22·922	55·520
12·545	151·22	13·445	127·60	11·011	121·92	21·818	102·73	17·015	57·683
9·7144	152·90	12·321	128·23	8·7616	123·20	15·505	106·55	15·178	58·054
8·1863	153·69	10·662	129·11	6·0398	125·28	10·881	110·16	10·613	60·105
7·3296	154·40	7·2590	131·18	4·7112	126·65	9·5736	111·03	7·5686	61·648
6·2305	155·29	6·4312	131·84	3·7006	127·74	7·2593	113·24	6·4043	62·255
4·4496	156·80	4·4029	133·53	2·2969	129·37	4·4323	116·63	5·5066	62·887
3·2844	157·61	2·4718	135·49	1·8118	129·80	3·8097	117·21	3·3066	64·461
1·8389	159·55	1·6574	136·66	0·77174	131·93	2·3430	119·30	2·3094	65·226
1·0065	160·95	1·3762	137·06	0·50590	132·52	1·9358	121·25	1·5985	66·198
0·33567	162·49	0·66736	138·41	0·34599	133·18	0·94702	122·76	0·92535	67·325
0·10210	163·40	0·33841	139·36	0·047712	134·49	0·28205	124·81	0·38423	68·097
						0·17620	125·63		

DISCUSSION

As with the similar series of salts measured by Walden and Birr,[3] the plots of Λ against $c^{0.5}$ for the various systems are almost linear over a concentration range up to 2×10^{-3}N for the tetra-alkylammonium picrates, and up to 3×10^{-3}N for the amine salts. In all cases the observed slope of the line is somewhat greater than the theoretical Onsager value, owing presumably to ion-pair association. Each of the five salts gave linear Fuoss plots ($c\Lambda f^2/F$ versus F/Λ) from which the limiting conductance Λ_0 and ion-pair dissociation

TABLE 2.

Picrates	Et_4N	Bu_4N	$(C_5H_{11})_4N$	$(CH_2Ph)_3NH$	$Ph{\cdot}NH_3$
Λ_0	164·5	141·2	135·2	126·5	70·0
10^4K	1508	706·8	339·8	144·4	—

TABLE 3.

Solvent	$CH_2{\cdot}CHCl_2$ [a]	$(CH_2Cl)_2$ [b]	$Ph{\cdot}NO_2$ [c]	MeOH [d]	$COMe_2$	MeCN [e]
$\Lambda_0\eta$	0·451	0·451	0·505	0·471	0·463	0·485
$\Lambda_0^{\frac{1}{2}}\eta$	0·206	0·206	0·212	0·202	0·204	0·207

[a] Healey and Martell, *J. Amer. Chem. Soc.*, 1951, **73**, 3296. [b] Ref. 6. [c] Taylor and Kraus, *J. Amer. Chem. Soc.*, 1947, **69**, 1731. [d] Evers and Knox, *ibid.*, 1951, **73**, 1739. [e] Reynolds and Kraus, *ibid.*, 1948, **70**, 1709. [f] This work.

constant K were computed. Relevant data are recorded in Table 2. At concentrations in excess of 10^{-3}N the slopes of the Λ–$c^{0.5}$ plots are less than required by theory, as is usually the case in systems of this type.

[12] International Critical Tables, Vol. I, McGraw-Hill Book Co. Inc., New York, 1926.

XUM

The limiting conductance of tetra-*n*-butylammonium picrate found in the present experiments may be used to compute the ion conductances of other tetra-*n*-alkylammonium ions in the same solvent. Table 3 shows that tetra-*n*-butylammonium picrate obeys Walden's rule fairly closely in a number of solvents, and a mean value of $0{\cdot}207 \pm 0{\cdot}005$ may be accepted for $\Lambda_0^+\eta$. Since the viscosity of acetonitrile at 25° is 0·0034376, it follows that Λ_0^+ should have the value 60·2 and, since $(\Lambda_0^+ + \Lambda_0^-) = 141{\cdot}1$, Λ_0^- for the picrate ion in this solvent must be 80·9. It is then possible to calculate limiting conductances for the whole series of tetra-*n*-alkylammonium ions by subtracting the value for the picrate ion (80·9) from the limiting conductance of the appropriate salt. By combining the present results with Walden and Birr's for tetramethylammonium and tetra-*n*-propylammonium picrate,[3] it can be seen from the second line of Table 4 that the cation conductances in acetonitrile decrease irregularly with increasing number of carbon atoms. Walden and Birr's values for the equivalent conductance of tetraethylammonium picrate, the only solute common to both investigations, are slightly but not significantly lower than ours over the whole range of concentration and result in a correspondingly slightly lower value of Λ_0 (163·8). The use of Walden and Birr's values of Λ_0 for the first three solutes referred to in Table 4, while giving a slightly different value for the increments as shown in the third line of the Table, do not alter the conclusions noted above. The reason for the

TABLE 4.

Cation	Me_4N	Et_4N	Pr_4N	Bu_4N	$(C_5H_{11})_4N$
Λ_0^+ difference	5·9	18·7	4·8	6·1	
Λ_0^+ difference (Walden)	6·7	17·9			

abnormally large decrease in conductance from ethyl to propyl is not fully understood, but is a phenomenon observed in certain other solvents also.

Fuoss and Elliott [1] and Witschonke and Kraus [13] have shown that some amine picrates exist in certain solvents as a mixture of molecularly and ionically dissociating species, and the low value of Λ_0 for aniline picrate obtained now can similarly be explained on the basis of two equilibria in acetonitrile :

$$C_6H_5{\cdot}NH_2Pic \rightleftharpoons C_6H_5{\cdot}NH_3^+ + Pic^- \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (a)$$

$$C_6H_5{\cdot}NH_2Pic \rightleftharpoons C_6H_5{\cdot}NH_2 + HPic \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (b)$$

The equilibrium constants of reactions (*a*) and (*b*) will be denoted by K and k respectively. A value of the true (ionic) limiting conductance was estimated in the following way. The limiting cation conductance Λ_0^+ is approximately a function of the number n of carbon atoms present. Λ_0^+ for tetramethylammonium ($n = 4$) and for tetraethylammonium ($n = 8$) in acetonitrile is 89·6 and 83·7 respectively, the latter value being somewhat smaller than expected. A value of 87·0 may therefore be adopted for anilinium ($n = 6$). Λ_0 for aniline picrate in acetonitrile at 25° will then be (87·0 + 80·9). When this value is used, a plot of $\frac{1}{f}\left(\frac{F}{\Lambda} - \frac{1}{\Lambda_0}\right)$ against $c\Lambda f/F$, where f is the mean ion activity coefficient and F the Fuoss function, is linear over a considerable concentration range. A slight deviation occurring in very dilute solution may possibly result from the rather large solvent correction (approx. 2%) applied in this region. The ionic and molecular dissociation constants evaluated from the slope and intercept of the linear portion of the plot were found to be $K = 10{\cdot}43 \times 10^{-4}$ and $k = 23{\cdot}46 \times 10^{-4}$. It is of interest to compare these values with the corresponding figures in nitrobenzene,[13] where $K = 0{\cdot}554 \times 10^{-4}$ and $k = 0{\cdot}163 \times 10^{-4}$. The difference is particularly striking since the dielectric constants of the two solvents are very similar (acetonitrile ε 36·2; nitrobenzene ε 34·5), and it illustrates the importance of solvent properties other than the dielectric constant in conductance phenomena. It is also worthy of note that k is larger than K in acetonitrile, indicating that the non-ionic

[13] Witschonke and Kraus, *J. Amer. Chem. Soc.*, 1947, **69**, 2472.

molecular dissociation predominates, although the reverse condition exists in nitrobenzene.

The Λ–$c^{0.5}$ plot for tribenzylammonium picrate was again linear over a considerable concentration range—at least up to $2{\cdot}5 \times 10^{-3}$N, with a slope slightly greater than theoretical, although it has been suggested elsewhere that this solute may be expected to behave as a weak electrolyte. Fuoss and Elliott,[1] on the other hand, observed that the picrates of the aromatic amines such as tribenzylamine also gave conductance curves suggesting that they exist, in certain solvents, in two modifications, one of which cannot furnish ions. This does not appear to be true for tribenzylamine picrate in acetonitrile however; or at most the ionic form appears to be present in very considerable excess. Thus the value of Λ_0 obtained from the Fuoss plot is 126·9, which gives $\Lambda_0^+ = 46{\cdot}0$ for the tribenzylammonium ion since Λ_0^- for the picrate ion is 80·9. It will be observed (Table 2), that the element of dissymmetry in the tribenzylammonium ion, as compared with the tetra-*n*-pentylammonium ion, has brought about a marked reduction in the dissociation constant. The relative importance of the two dissociation processes discussed above with reference to aniline picrate and tribenzylamine picrate is clearly dependent both on the structure of the ions involved and on the nature of the solvent medium. This suggests that solvent–solute interaction, which is specifically ignored in the current theory of conductivity, may be an important factor in conductance processes.

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409. *The Interpretation of Soret-effect Measurements on Aqueous Electrolyte Solutions by the Tanner Method.*

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Calculation of Soret coefficients from optical measurements of the refractive-index gradients within a pure Soret effect cell by Tanner's method [1,2] is subject to several possible errors. These have been examined in the light of new experimental results for a range of salt solutions. In particular, it appears that the recorded temperature interval across the cell may have been too high, and the calculated Soret coefficients too low, in some earlier work. Averaging the refractive-index gradients across the cell instead of using the values obtaining at the centre of the cell has a similar effect. Revised Soret coefficients and heats of transfer are tabulated for a number of salt solutions.

AN important method of studying the thermal migration (pure Soret effect) occurring in a column of liquid in which a vertical temperature gradient exists is to measure the change in refractive-index gradient along the column, conveniently by Tanner's method [1,2] in which the deviation of a narrow beam of parallel light during its passage through the cell is observed. This deviation affords the refractive-index gradient at any horizontal plane in the cell; this gradient is an average value over a small vertical distance within the column of liquid, since the beam has a finite width and leaves the cell at a lower level than that at which it enters. Tanner's optical system, based on Thovert's,[3] was such that this

[1] Tanner, *Trans. Faraday Soc.*, 1927, **23**, 75.
[2] *Idem, ibid.*, 1953, **49**, 611.
[3] Thovert, *Ann. Chim. Phys.*, 1902, **26**, 366; 1914, **2**, 369.

average gradient could be obtained simultaneously at a number of horizontal planes within the cell, by measuring the deflection (from a suitable reference line) of successive points along a slit image. When the column is isothermal, the image is horizontal, one end corresponding to the upper and the other to the lower boundary surface of the column. If the upper end of the column is heated, the whole image is shifted rapidly downwards to form initially a displaced image, horizontal in the centre, with the tips bent upwards or, more often, downwards. Usually, there is a slow further displacement as the concentration changes in the solution, until the steady-state equilibrium is established. The final image is approximately horizontal, and displaced uniformly from the initial isothermal image.

The experimental quantities are the observed displacements of successive points on the slit image as a function of time and position in the cell, and the temperature interval between the upper and lower boundary surfaces of the column of solution. In principle, these can be used to calculate: (a) An ordinary diffusion coefficient D, which is an average value over a small temperature range. This may be obtained from the rate at which any given point on the image is displaced after the initial rapid displacement due to the temperature gradient.[2,4] (b) The ratio D'/D of the thermal coefficient D' to the ordinary diffusion coefficient, most satisfactorily defined as:

$$\frac{D'}{D} = \frac{1}{N_1(1-N_1)}\left(\frac{\mathrm{d}N_1}{\mathrm{d}T}\right)_{\text{stat.}} = -\frac{1}{N_2(1-N_2)}\left(\frac{\mathrm{d}N_2}{\mathrm{d}T}\right)_{\text{stat.}} = -\frac{1}{m}\left(\frac{\mathrm{d}m}{\mathrm{d}T}\right)_{\text{stat.}}$$

where N_1 is the mole fraction of solvent, N_2 that of solute, m the molality of the solution, and the differential terms are the concentration gradients when the final steady state has been reached.

Some time ago, through the courtesy of Dr. C. C. Tanner, it became possible to study the Soret effect in a number of electrolyte solutions of interest in connection with other work on non-isothermal systems. Since then advances have been made in the descriptive theory of the pure Soret effect, and on re-examining these experimental results it became clear that care is necessary in converting them into values of D'/D. Tanner, in his earlier work, measured the displacement of what he termed the " crest " of the curved slit image relative to the position of the image when the contents of the cell were isothermal. That is, he measured the central, initially straight portion and ignored the curved ends of the image. He was only interested in the final displacement in the steady state and obtained this by empirical extrapolation from the " crest displacements " in the later stages of the experiment. Unfortunately the results are expressed in the form $c^{-1}(\mathrm{d}c/\mathrm{d}T)_{\text{stat.}}$ where c is the molarity of the solution. It is necessary therefore to convert his data on to a molality basis before values of D'/D can be obtained.[5] In his second paper,[2] the principal aim was the calculation of D from the rate of the displacement of the image before the establishment of the steady state; an approximate solution [6] of the differential equation governing the thermal migration process was used; this does not predict the observed curvature of the image at the edges, and Tanner therefore calculated an *average* displacement of the beam from his observations. If $Y_{\xi t}$ is the displacement at time t of the image point corresponding to the light passing through the cell, of total height a, at a level x above the base ($\xi = x/a$), the mean displacement calculated from observations at r points along the image is $r^{-1}\Sigma Y_{\xi t}$. A simple application of the de Groot equation suggests that:

$$\frac{r_1^{-1}\Sigma Y_{\xi t} - r_2^{-1}\Sigma Y_{\xi\infty}}{r_3^{-1}\Sigma Y_{\xi T} - r_2^{-1}\Sigma Y_{\xi\infty}} = \exp(-t/\theta)$$

where $Y_{\xi T}$ and $Y_{\xi\infty}$ are the displacements at an image point corresponding to the horizontal plane ξ, at the time T when the temperature gradient has just been fully established,

[4] Tyrrell, *Trans. Faraday Soc.*, 1956, **52**, 940.
[5] Alexander, *Z. phys. Chem.* (*Leipzig*), 1954, **203**, 181.
[6] de Groot, " L'Effet Soret," North Holland Publ. Co., Amsterdam, 1945.

and in the steady state respectively, and t is the time elapsed since the system ceased to be isothermal. θ is a " characteristic time constant " for the apparatus defined by $a^2/\pi^2 D$. In fact, θ is found not to be constant unless the observed differences in the mean displacements at time t and at time ∞ are adjusted by means of a small additive or subtractive constant, the " bias correction." Apart from the " bias correction," the effect of the averaging process is usually such that

$$r_3^{-1}\Sigma Y_{\xi T} - r_2^{-1}\Sigma Y_{\xi\infty} < Y_{0\cdot5,T} - Y_{0\cdot5,\infty}$$

where $Y_{0\cdot5,T}$ is the displacement at the centre of the cell immediately after the establishment of the temperature gradient. Since the ratio D'/D is calculated from this final difference, Tanner's second method of calculation should normally give lower results than his first. In fact it can be shown [4] that the first is more correct. The image displacement at the centre of the cell remains almost constant, and equal to that arising from the temperature gradient alone, as long as the time t elapsed since the application of the temperature gradient remains less than $0{\cdot}1\theta$. It can be shown graphically by the Schmidt method [7] that the uniform temperature gradient was established within 1 minute in all the present experiments on the determination of the Soret coefficient. Since θ is usually of the order of 70—100 minutes for aqueous electrolytes, an observation of the constant deflection at the centre of the image between 2 and 7 min. from the commencement of the experiment gave a measure of the temperature gradient within the cell. Thus, if attention is confined to the displacements at the centre of the exploring beam, the temperature and concentration effects can easily be separated.[8]

In order to obtain D'/D from the measured displacements it is usually considered sufficient to know $(\partial\mu/\partial w)_T$ (where μ is the refractive index of the solution and w the concentration), and the temperature interval across the cell as recorded by some conventional device. Tanner, for example, used a pair of calibrated mercury-in-glass thermometers. The refractive index of a solution varies with the concentration of the solute approximately according to the equation : [9]

$$\mu - \mu_0 = aw + bw^2 + cw^3 + \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (1)$$

where μ_0 is the refractive index of the solvent, w the concentration, and a, b, c, etc., are empirical constants. Tanner limited the series to two terms, and obtained on differentiation

$$(\partial\mu/\partial w)_T = a + 2bw \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (2)$$

He expressed w as the molar fraction of solute, and obtained a and b by measuring the refractive index of the solution whose Soret effect had been studied, of a solution of half this concentration, and of the solvent. Since eqn. (1), and more so eqn. (2), is not exact it is desirable to examine the magnitude of the error introduced by this procedure. It is also possible that the measured temperature interval τ_M may be more or less high. This can easily be tested if $(\partial\mu/\partial T)_w$ is known for the solution. The initial constant displacement at the centre of the slit image is proportional to $(\partial\mu/\partial T)_w \cdot \tau$ and hence the true value of τ at the start of the experiment may be found.

The measurements on electrolyte solutions available to us have been examined in the light of the above considerations and it has been shown that there is a tendency to underestimate the correct value of D'/D corresponding to a given set of experimental results. The best values of this quantity have been calculated for a number of electrolyte solutions, and these, where possible, have been converted into values of the heats of transfer.

[7] Ingersoll, Zobell, and Ingersoll, " Heat Conduction," McGraw-Hill Book Co., New York, 1948, p. 209; cf. Tanner, " The Soret Effect," Part II, I.C.I. Central Agricultural Control Report, August, 1952.
[8] Thomaes, *Physica*, 1951, **17**, 885.
[9] Partington, " Advanced Treatise on Physical Chemistry," Longmans, Green and Co., London, 1953, Vol. IV, p. 76.

Experimental

Soret effects were measured at 25—35° in Dr. Tanner's laboratory, the apparatus and techniques described by him [2] being used. Almost all the values of $d\mu/dm$ used were obtained from measurements at 30° on a Hilger-Chance refractometer, with a V cell for liquids and the green mercury line (5461 Å). Temperature coefficients of refractive index were obtained later with a Zeiss Pulfrich refractometer, from measurements of refractive index at 26° and 34°, with the same light source except where otherwise stated. No special precautions were taken in these experiments, and the temperature of the solution in the cell was assumed to be that of the circulating water in the refractometer. The accuracy of the measurements was checked with distilled water, and with " AnalaR " benzene dried over sodium. With the sodium *D* line as source, $\Delta\mu/\Delta T$ was found to be $-11{\cdot}4 \times 10^{-5}$ deg.$^{-1}$ for water; Flatow [10] found $-11{\cdot}54 \times 10^{-5}$ at 30°. For benzene, a value of -61×10^{-5} deg.$^{-1}$ was obtained. Between 10° and 30° Weegman [11] found $-64{\cdot}5 \times 10^{-5}$, and between 20° and 30° $-63{\cdot}2 \times 10^{-5}$. Measurements on salt solutions were repeated several times, and the mean values obtained (Table 1) are not more than 2—3% in error. This accuracy is adequate for the present purpose.

The salts used were selected because of their relevance to certain other problems and not as part of a systematic programme of work on the Soret effect. The reason for the choice of quaternary halides will be clear from the following paper.

Tetramethyl- and tetraethyl-ammonium bromides (from B.D.H.) were purified by dissolution in absolute alcohol and precipitation with ether after filtration. The other substituted ammonium salts used were chosen partly because of their accessibility. *NNN*-Trimethylanilinium bromide was prepared by treating ethyl α-bromopropionate with dimethylaniline at 160° for 8 hr.[12] and purified as described above (Found : Br, 37·2. Calc. for $C_9H_{14}NBr$: Br, 37·0%). 1-Ethylpyridinium bromide was prepared by refluxing pure pyridine with excess of dry ethyl bromide for 30 min., cooling, filtering, and dissolving the solid salt in absolute alcohol.[13] Precipitation with ether gave a high yield of the deliquescent salt (Found : Br, 42·8. Calc. for $C_7H_{10}NBr$: Br, 42·6%). The analytical discrepancy was probably due to the absorption of water. 1-Ethylquinolinium iodide was made [14] by warming quinoline with excess of dry ethyl iodide : excess of ethyl iodide was distilled off the solid yellow product, which was then purified in the usual manner (Found : I, 44·5. Calc. for $C_{11}H_{12}NI$: I, 44·5%). Sodium, potassium, silver, barium, and ammonium nitrate, and potassium bromide and iodide solutions, were made from dried " AnalaR " reagents in redistilled water. Magnesium nitrate solution was prepared by adding excess of dry " AnalaR " magnesium oxide to a known amount of pure pure nitric acid, filtration, and dilution. Commercial lithium hydroxide was used without purification.

Results and Discussion

Errors in the Determination of $d\mu/dm$.—If μ can be expressed as a quadratic function in m (molality) the quantity $(\mu - \mu_o)/m$ should be a linear function of m. For aqueous silver nitrate this is not quite correct (see Figure, where the straight line was obtained from the experimental points by the method of least squares). If

$$(\mu - \mu_o)/m = a + bm,$$

then

$$[(\mu - \mu_o)/m]/dm = b$$

and

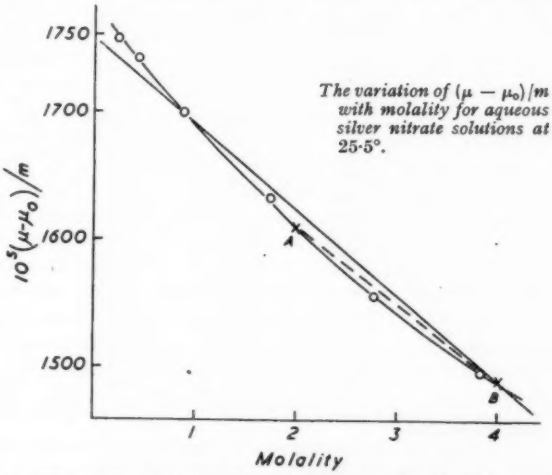
$$d\mu/dm = mb + (\mu - \mu_o)/m$$

If the " least squares " line is used in calculating $d\mu/dm$, the result will be in error for two reasons. The quantity b differs appreciably from the slope of the experimental curve except in the 2—3 molal region, where the estimate of $(\mu - \mu_o)/m$ is most seriously in error. This error in $[(\mu - \mu_o)/m]$ is not greater than about 1% at worst. The largest error introduced by using the " least squares " line, *i.e.*, by assuming μ to be simply a quadratic function of m, rather than the experimental curve, occurs at the higher concentrations

[10] Flatow, *Ann. Physique*, 1903, **12**, 85.
[11] Weegman, *Z. phys. Chem.*, 1888, **2**, 237.
[12] Bischoff, *Ber.*, 1898, **31**, 3017.
[13] Trowbridge and Diehl, *J. Amer. Chem. Soc.*, 1897, **19**, 563.
[14] Dehn and Cope, *ibid.*, 1926, **48**, 2636.

where the slopes of the curve and the straight line diverge most markedly. At 4 molal, the error in calculating $d\mu/dm$ from the line rather than the curve is of the order of 4%. However, the method of estimating $d\mu/dm$ used by Tanner (see above) introduces a smaller error than this, since it is equivalent to substituting the chord *A*—*B* for the tangent to the curve at *B*. Since other, larger sources of error are inherent in the Tanner method this procedure has been used in the present work.

Measurement of the Temperature Interval in Soret-effect Experiments.—The temperature interval in the cell immediately after the establishment of the uniform temperature gradient (τ_C) has been calculated from the experimental values of $\Delta\mu/\Delta T$, and the deflection of the central portion of the slit image measured between 2 and 7 min. after the start



The variation of $(\mu - \mu_0)/m$ with molality for aqueous silver nitrate solutions at 25·5°.

of the experiment. The value obtained has been compared with that recorded on the mercury-in-glass thermometers. The bulbs of these were placed in pockets, the ends of which were formed by the back surfaces of the silver plates forming the upper and the lower boundary surface of the cell. The quantities τ_M are the temperature intervals

TABLE 1. *Comparison of observed and calculated temperature intervals in Tanner Soret-effect cell for different aqueous electrolytes.*

Solute	Molality	$10^5\,\Delta\mu/\Delta T$ (deg.$^{-1}$)	τ_M	τ_C	Solute	Molality	$10^5\,\Delta\mu/\Delta T$ (deg.$^{-1}$)	τ_M	τ_C
$NaNO_3$ ...	4·625	−19	9·78	8·5	$Ba(NO_3)_2$ ...	0·386	−13	10·25	9·6
	2·153	−17	9·88	9·0	KBr	2·204	−15	9·98	8·5
KNO_3.....	3·405	−17	9·88	8·9	KI	2·203	−17	10·02	14·6
	2·159	−16	9·91	8·8	NMe_4Br.....	2·514	−14	9·95	9·1
NH_4NO_3	5·037	−19	9·95	8·7		1·135	−13	9·97	9·1
	2·794	−16	9·92	9·9	NEt_4Br ...	1·801	−14	9·92	9·9
$AgNO_3$ ...	2·130	−15	9·60	9·1	1-Ethylquinolinium iodide	0·517	−13	10·04	9·0
	0·393	−13	10·58	8·9					

recorded on these thermometers after stem corrections had been applied. The results are shown in Table 1. Obviously τ_C should not be greater than τ_M and the only exception to this was found with potassium iodide solution where the initial deflection was unusually large. Surprisingly, τ_C was usually appreciably less than τ_M, *i.e.*, the temperature gradient within the cell at the beginning of the experiment corresponded to a smaller temperature interval than that recorded on the thermometers. This conclusion was re-inforced by an experiment in which the cell was filled with distilled water and the temperature gradient applied. A value for $\Delta\mu/\Delta T$ of $-9{\cdot}8 \times 10^{-5}$ deg.$^{-1}$ (λ 5461 Å) was calculated from the

observed image deflection (which was independent of ξ) and the measured temperature interval. This was appreciably less than it should have been. At 30°, at λ 4800 Å, $d\mu/dT = -11{\cdot}82 \times 10^{-5}$, and at λ 5890 Å, $d\mu/dT = -11{\cdot}54 \times 10^{-5}$ deg.$^{-1}$ (ref. 10). The temperature gradient in this experiment was undoubtedly uniform across the cell and less than that indicated by the thermometers.

Values of $\bar{p}$ and D'/D.— $\bar{p}(=\tau D'/D)$ can be calculated from experimental measurements without introducing any difficulties connected with the correct value of the temperature interval τ. Table 2 shows values of this quantity obtained: (i) ($\bar{p}_1$) by Tanner's

TABLE 2. *Calculation of $\tau D'/D$ by various methods, and estimates of D'/D.*

Salt	Molality	$10^3\bar{p}_1$ (cm.)	$10^3\bar{p}_2$ (cm.)	$10^3\bar{p}$ (cm.)	$10^3 D'/D$ (deg.$^{-1}$)
$NaNO_3$	4·625	26·6	25·8	25·8	3·0
	2·153	19·1	18·2	19·0	2·1
KNO_3	3·405	37·6	37·4	41·2	4·6
	2·159	22·7	21·8	24·7	2·8
NH_4NO_3	5·037	5·62	5·62	5·9—6·4	0·7 *
	2·794	No Soret effect observed			
$AgNO_3$	2·130	57·0	55·9	74·0	8·1
	0·393	27·8	27·2	36·0	4·0
$Ba(NO_3)_2$	0·386	37·8	37·8	41·2	4·3
$Mg(NO_3)_2$	2·143	No Soret effect observed			
LiOH	4·473	31·9	31·9	37·6	3·8 †
KBr	2·204	11·6	11·9	15·3	1·8
KI	2·203	6·27	6·10	6·33	0·63 †
NMe_4Br	2·514	49·0	48·5	59·5	6·5
	1·135	38·8	40·2	41·6	4·6
NEt_4Br	1·801	81·6	80·1	86·9	8·7
1-Ethylquinolinium iodide	0·517	100·4	100·2	106·6	12 ‡
1-Ethylpyridinium bromide	2·015	51·0	51·0	51—58	5·1—5·8 *
$NPhMe_3Br$	0·533	59·6	59·1	70·2	7·0

* The displacement of the central image varied in these cases over a short distance and the choice of a unique value was impossible.

† Calc. from τ_M rather than τ_C. Apart from KI this was because no value of $\Delta\mu/\Delta T$ was available.

‡ The steady state equilibrium had not been completely attained.

averaging method, modified to include the " bias correction " in the average value of the final beam displacement; (ii) ($\bar{p}_2$) as in (i) but omitting the " bias correction " (this appears to have been the method used in his later work by Tanner); and (iii) from the deflection at the *centre* of the image, this being termed $\bar{p}$ and being the correct quantity to use in the calculation of D'/D.

Calculation of D'/D from $\bar{p}$ involves the problem of the correct value of the temperature interval discussed in the previous section. The values shown in Table 2 have been calculated, except where otherwise stated, from τ_C. The calculation is slightly complicated because the measured temperature interval may change by a small amount during the long period required for the establishment of the steady state. The change in τ_C due to this slight drift has been assumed to be proportional to that in τ_M.

The experimental values of $\bar{p}_1$ and $\bar{p}_2$ are, to some extent, subjective quantities. It is never possible to observe the whole image throughout an experiment; the portion whose position can be recorded varies during a given experiment, and from one experiment to another. Thus, in different runs the relative weights given to the observations at the centre and to those at the ends of the slit image will vary, and the " average displacements " will not be strictly comparable. Usually, though not invariably, they were less than that at the centre of the image, and values of D'/D calculated from either $\bar{p}_1$ or $\bar{p}_2$ are likely to be lower than the true value. Thus Tanner's latest values [2] for potassium and barium chloride solutions are probably too low. The Soret coefficients recorded in the earlier paper,[1] if corrected to a molality basis, are undoubtedly more correct. They may still be less than the true values however, because of the possibility that the temperature interval had been over-estimated (see above).

Calculation of Heats of Transfer from D′/D.—The heats of transfer of the ions of a completely dissociated binary electrolyte is related to D'/D by the equation : [15]

$$(\nu_+Q_+^* + \nu_-Q_-^*) = \nu RT^2[1 + m(\partial \ln \gamma_\pm/\partial m)_{Tp}] \cdot D'/D$$

where ν_+ and ν_- are the numbers of positive and negative ions and ν is the total number of ions per molecule. The activity coefficient on the molality scale is known for many salts at 25°, and $m(\partial \ln \gamma_\pm/\partial m)_{Tp}$ can be obtained graphically from these results without serious error. In the present experiments the mean temperature was 30°. The change in $m\partial \ln \gamma_\pm/\partial m$ with temperature is given by :

$$m \cdot \frac{\partial}{\partial T}\left(\frac{\partial \ln \gamma_\pm}{\partial m}\right) = m \cdot \frac{\partial}{\partial m}\left(\frac{\partial}{\partial T} \cdot \ln \gamma_\pm\right) = -\frac{m}{\nu RT^2} \cdot \frac{\partial \bar{L}_2}{\partial m}$$

where $\bar{L}_2$ is the relative partial molar heat content of the solute. For a 2 molal potassium bromide solution, this is about -18×10^{-4} deg.$^{-1}$, the heat data of Hammerschmid and Robinson [16] being used. The change in $m\partial \ln \gamma_\pm/\partial m$ for a temperature change from 25° to 30° is about −0·009 which corresponds to a change in the term $[1 + m\partial(\ln \gamma_\pm)_{Tp}/\partial m]$ of about 1%. Therefore, except for substances with exceptionally large heats of dilution, the error in using activity coefficients obtained at 25° instead of at 30° is small compared with the uncertainty in D'/D (see also Chapman and Tyrrell [17]).

Values of the quantity $(\nu_+Q_+^* + \nu_-Q_-^*)$ calculated from values of D'/D and from published activity coefficient values [18] are shown in Table 3. There is no extensive series of similar values with which these can be compared exactly. That calculated by Alexander [19] from Tanner's earlier values refers to slightly higher mean temperatures : he calculated mean heats of transfer $Q_\pm^*$ defined for a uni-univalent electrolyte as $(\nu_+Q_+^* + \nu_-Q_-^*)/\gamma$, and his tabulated values should therefore be doubled for comparison with the data of Table 3. There is a slight error in Alexander's definition of the heat of transfer since equation (3) of this paper should read $s_\pm = x^{-1}(1 - x) \cdot \text{grad } x/\text{grad } T$, not $s_\pm = x^{-1}(1 - \nu x) \cdot \text{grad } x/\text{grad } T$. Consequently his values are slightly higher than they should be (1% in error at 1 molal, 4% in error at 2 molal, 6% at 3 molal, and 7·5% at 4 molal for a uni-univalent electrolyte). After this small correction his values are somewhat larger than the present ones. Qualitatively, this would be expected, for heats of transfer increase with temperature,[5] but too little is known at present about the magnitude of this change for a quantitative comparison between the two sets of values to be possible. In some cases the difference is rather greater than might reasonably be expected from this cause alone.

Calculation of the Ordinary Diffusion Coefficient D.—This calculation was done for a number of the above solutions both by Tanner's method [2] and by the method described recently by one of us.[4] As in the case of 2·2 molal potassium bromide there examined, the two methods gave similar but not identical results. The values obtained were all of the right order of magnitude ($\sim 10^{-5}$ cm.^{2} sec.$^{-1}$) but in many cases reliable isothermal data for comparison do not exist. The error in the second method could be estimated from the variation of the values of the characteristic time θ calculated from successive observations. This appeared to be of the order of 3—4% at least, even in the most favourable cases.

Conclusions.—There seems no doubt that this optical method of measuring Soret coefficients in the form described by Tanner [2] may give low results, for two reasons. The method of averaging displacements across the cell usually yields a mean value lower than the correct one measured at the centre of the cell. In addition, there is considerable evidence that, in certain experiments, though not in all, the temperature interval recorded

[15] Haase, *Trans. Faraday Soc.*, 1953, **49**, 724.
[16] Hammerschmid and Robinson, *J. Amer. Chem. Soc.*, 1932, **54**, 3120.
[17] Chapman and Tyrrell, *Trans. Faraday Soc.*, 1956, **52**, 1218.
[18] Robinson and Stokes, "Electrolyte Solutions," Butterworths, London, 1955.
[19] Alexander, *Z. phys. Chem.* (*Leipzig*), 1954, **203**, 228.

TABLE 3. $(\nu_+Q_+^* + \nu_-Q_-^*)$ *at a mean temperature of* 30°, *calculated from values of* D'/D *obtained in Table* 2.

Salt	Molality	$1 + m(\partial \ln \gamma_\pm/\partial m)$	$(\nu_+Q_+^* + \nu_-Q_-^*)$ (cal. mole^{-1})
$NaNO_3$	4·625	0·743	800
	2·153	0·793	610
KNO_3	3·405	0·418	700
	2·159	0·525	540
NH_4NO_3	5·037	0·529	130
	2·794	—	zero
$AgNO_3$	2·130	0·480	1400
	0·393	0·750	1100
$Ba(NO_3)_2$	0·386	0·515	1200
$Mg(NO_3)_2$	2·143	—	zero
LiOH	4·473	0·884	1200
KBr	2·204	1·000	660
KI	2·203	1·048	240

on the mercury-in-glass thermometers was greater than that between the upper and the lower boundary surface of the liquid column. Both errors would combine to give low values for D'/D. The first was not operative in Tanner's earlier work;[1] the second may have been, though its influence cannot be judged from the published data. In any event, its magnitude would be expected to vary from experiment to experiment, since it would depend largely on the goodness or otherwise of the thermal contact between the thermometer bulb and the metal parts of the experimental cell. A better method of measuring the initial thermal gradient would undoubtedly be that used here, *viz.*, measurement of the initial displacement of the centre of the beam image from its original position when the cell was isothermal, provided that more accurate values of $(\partial\mu/\partial T)_m$ could be obtained.

We are indebted to Imperial Chemical Industries Limited and Dr. C. C. Tanner for provision of facilities at the Hawthorndale Laboratories where the Soret-coefficient measurements were carried out, and to the University of Sheffield for the award of post-graduate research scholarships (to J. C. and P. J. W.).

THE UNIVERSITY, SHEFFIELD. [*Received, October 25th,* 1956.]

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410. *Measurements on Thermocells containing Dilute Solutions of Quaternary Ammonium Bromides as Electrolytes.*

By J. CHAPMAN and H. J. V. TYRRELL.

Differences in the thermoelectric powers of thermocells with silver–silver bromide electrodes and dilute aqueous solutions of quaternary ammonium bromides as electrolyte, have been measured for a series of such salts. The results, together with those of some direct Soret coefficient measurements described in the preceding paper, do not support the values for the entropies of transfer of single ions suggested by Goodrich *et al.*[1] on the basis of measurements of thermoelectric power alone.

THE initial electrical potential gradient $(d\phi/dT)_{sol.}$ associated with the presence of a thermal gradient in an electrolyte solution of uniform concentration can be expressed (for a uni-univalent salt) as:

$$-FT\,(d\phi/dT)_{sol.} = t_+Q_+^* - t_-Q_-^* \quad . \quad . \quad . \quad . \quad . \quad . \quad (1)$$

where t_+ and t_- are the transport numbers, and Q_+^* and Q_-^* the heats of transfer of the positive and the negative ions respectively.[2] These ionic heats of transfer are not experimentally accessible, though they can be obtained in combination. For example, when the

[1] Goodrich, Goyan, Morse, Preston, and Young, *J. Amer. Chem. Soc.*, 1950, **72**, 4411.
[2] Haase, *Trans. Faraday Soc.*, 1953, **49**, 724.

steady state is reached in such a system, a constant and characteristic concentration gradient coexists with the temperature gradient, and

$$\frac{1}{m}\left(\frac{\mathrm{d}m}{\mathrm{d}T}\right)_{\text{stat.}} = -\frac{Q_+^* + Q_-^*}{2RT^2}\left(1 + \frac{\partial \ln \gamma_\pm}{\partial m}\right) \equiv -\frac{Q_\pm^*}{RT^2}\left(1 + \frac{\partial \ln \gamma_\pm}{\partial m}\right)$$

where m is the molality of the solution. It is possible in principle to measure $m^{-1}(\mathrm{d}m/\mathrm{d}T)_{\text{stat.}}$ and to obtain $(Q_+^* + Q_-^*)$ as was done, for example, in the preceding paper. The problem of apportioning $(Q_+^* + Q_-^*)$ between individual ions has attracted some attention.[1,3,4] One recently published attempt [1] to do this was based on work carried out under the late Professor Eastman in California, on the initial thermoelectric powers of the cells :

$$\underset{20°}{\mathrm{Ag,AgBr|NR_4Br\ in\ water|}}\underset{30°}{\mathrm{AgBr,Ag}}$$

$$\underset{20°}{\mathrm{Hg,HgO|NR_4OH\ in\ water|}}\underset{30°}{\mathrm{HgO,Hg}}$$

R was a *n*-alkyl group, and experiments were carried out with successive members of the series up to the tetra-*n*-pentylammonium compound. The experiments were said to prove that the heats of transfer of large tetra-*n*-alkylammonium ions tended to a constant value, and a kinetic argument was used to justify the conclusion that this constant value was zero. On this basis a table of individual ionic entropies of transfer was compiled. These can be tested by using them to calculate $m^{-1}(\mathrm{d}m/\mathrm{d}T)_{\text{stat.}}$ from eqn. (2). This calculation depends only on the assumption that the heats of entropies of transfer of these large ions tend to a constant value and is independent of the further assumption that they tend to zero. The suggested values of the heats of transfer predict that, for the alkali bromides, the solute should concentrate at the heated end of the solution in 0·01 molal solution.[5] This is not in accord with experience on more concentrated solutions, as can be seen for example from the previous paper and elsewhere.[6] They also predict that the tetra-*n*-alkylammonium bromides should show a negligible Soret effect. The present paper describes some measurements, similar to those made by Goodrich *et al.*,[1] on the initial thermoelectric powers of cells with silver–silver bromide electrodes and solutions of quaternary ammonium bromides as the electrolyte. These are used, in combination with some of the Soret-effect measurements of the previous paper, to examine the validity of the ionic entropies of transfer suggested by Goodrich *et al.*

Experimental

The method used for measuring mean thermoelectric powers between 27° and 32° was based on that described earlier,[7] the cell being modified to permit preliminary saturation of the electrolyte with nitrogen pre-heated to the temperature of the electrolyte and saturated with water vapour by preliminary passage through a solution of potassium bromide of the same concentration as that of the electrolyte in the cell. This procedure has been previously recommended for work with substituted ammonium salts in order to prevent deterioration of the electrode system.[1] The nitrogen stream was interrupted while the e.m.f. measurements were made. Silver–silver bromide electrodes were made as described elsewhere.[8]

Transport numbers of the substituted ammonium cations were obtained by calculating limiting ionic mobilities from conductivity measurements. These were carried out at 25°, with a conventional A.C. Wheatstone bridge with a telephone detector. No correction for changes in the transport number with concentration has been applied, nor for the difference between the mean temperature of the thermocell and the temperature at which these measurements were carried out.

[3] Eastman, *J. Amer. Chem. Soc.*, 1926, **48**, 1482; 1928, **50**, 283, 292.
[4] Wirtz, *Z. Physik*, 1948, **124**, 482.
[5] Tyrrell and Hollis, *J. Amer. Chem. Soc.*, 1951, **73**, 2401.
[6] Tanner, *Trans. Faraday Soc.*, 1927, **23**, 75.
[7] Tyrrell and Hollis, *ibid.*, 1952, **48**, 893.
[8] Chapman and Tyrrell, *ibid.*, 1956, **52**, 1218.

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The quaternary ammonium salts, except tetra*iso*pentylammonium bromide, were prepared as described in the preceding paper. Tetra*iso*pentylammonium iodide was prepared by refluxing an excess of *iso*pentyl iodide with tri*iso*pentylamine in dry acetone for 10 hr. After removal of the acetone and cooling, colourless plates of the salt crystallised. Further quantities were obtained by adding acetone and refluxing again. The crystals were purified by dissolution in acetone and reprecipitation with ether. The bromide was prepared in solution by treating a suspension of the iodide with silver oxide and neutralising it with hydrobromic acid to pH 7.

Careful purification of these quaternary salts was essential before use in thermocells. For all salts except the ethylquinolinium bromide, dissolution in absolute alcohol and precipitation with ether, repeated several times, was sufficient. The ethylquinolinium bromide required three crystallisations from absolute alcohol at the temperature of acetone–solid carbon dioxide.

Results and Discussion

Values [7] of the function $P\ [\mathrm{d}\phi/\mathrm{d}T - 2{\cdot}303\boldsymbol{R}/z_r\boldsymbol{F} \log m_r + 2{\cdot}303\boldsymbol{R}/z_r\boldsymbol{F}(0{\cdot}8\sqrt{I})]$ calculated from the measured thermoelectric power $\mathrm{d}\phi/\mathrm{d}T$ of the cell: $\mathrm{Ag,AgBr|MBr\ in\ H_2O|AgBr,Ag}$ are in Table 1 for 0·01 and 0·10 molal solutions. The cation transport numbers in this Table (apart from those obtained from ref. 1) were calculated by extrapolating measured values of the equivalent conductivities of the quaternary ammonium bromide or iodide to infinite dilution, and assuming the limiting ionic mobility at 25° of the bromide ion to be 78·4 mho l. mole^{-1}, and that of the iodide ion to be 76·85. Tetra*iso*pentylammonium iodide was used in these experiments because the bromide is hygroscopic. These results agree with published values. For example, the cation transference numbers at infinite dilution for tetramethyl-, tetraethyl-, and tetra*iso*pentyl-ammonium cations can be calculated from earlier measurements [9] to be 0·37, 0·30, and 0·17 respectively. The values derived from ref. 1 however differ slightly, probably because they were calculated from a conductivity measurement at a single concentration (0·01 molal).

It has been shown [10] that, for a series of univalent salts with a common anion (say bromide), it is possible to write, ignoring deviations from ideality,

$$\sigma_{\mathrm{NBr}} = -\frac{\boldsymbol{F}}{2\boldsymbol{RT}}\frac{(P_{\mathrm{KBr}} - P_{\mathrm{NBr}})}{t_{\mathrm{N}}} + \frac{t_{\mathrm{K}}}{t_{\mathrm{N}}}\cdot\sigma_{\mathrm{KBr}} = \alpha + \beta\sigma_{\mathrm{KBr}}$$

where σ_{NBr} and σ_{KBr} are the Soret coefficients ($-Q_{\pm}^{*}/\boldsymbol{RT}^2$) of a salt NBr and of the reference substance KBr; P_{KBr} and P_{NBr} refer to values of the P function calculated from thermoelectric power experiments with KBr and NBr, respectively, as the electrolyte; and t_{K} and t_{N} are the transport numbers of the potassium ion and the cation $\mathrm{N^+}$. The derived quantity P varied slightly with concentration, and values derived from experiments on both 0·01 molal and 0·10 molal solutions, the corresponding values of α- together with the experimental transport numbers at infinite dilution and their ratios β, are shown in Table 1. This Table also includes data from Goodrich *et al.*[1]. The present measurements, obtained at a slightly higher mean temperature, are consistently lower than these where comparison is possible. However the differences, between the results from a given pair of compounds are almost identical.

Soret coefficients can be calculated from these results if a suitable value for the Soret coefficient of potassium bromide is known. From the preceding paper, 2·2 molal potassium bromide has a Soret coefficient of $-1{\cdot}8 \times 10^{-3}$ deg.$^{-1}$. At 0·05 molal and the same mean temperature (30°), Alexander [11] found $-1{\cdot}12 \times 10^{-3}$ deg.$^{-1}$. Unpublished measurements on an 0·01 molal solution with a novel conductometric method [12] have given $-1{\cdot}23 \times 10^{-3}$ deg.$^{-1}$ at 25°, and $-2{\cdot}18 \times 10^{-3}$ at 34·7°. If a value of about $-1{\cdot}5 \times 10^{-3}$

[9] Bencowitz and Renshaw, *J. Amer. Chem. Soc.*, 1925, **47**, 1904; Kraus and Fuoss, *ibid.*, 1933, **55**, 25; Landolt–Börnstein, Tabellen, Suppl. IIIc, p. 2059.
[10] Tyrrell and Colledge, *Trans. Faraday Soc.*, 1954, **50**, 1056.
[11] Alexander, *Z. phys. Chem.* (*Leipzig*), 1954, **203**, 213.
[12] Personal communication from Dr. J. N. Agar.

deg.$^{-1}$ is chosen for potassium bromide in 0·01 and 0·1 molal solution at a mean temperature of 30°, approximate coefficients may be calculated for the quaternary ammonium

TABLE 1. *Values of the function P, and of the constants α and β for quaternary ammonium bromides.*

Cation	Transport number of cation at inf. diln.	β	0·01 Molal P (μv/deg.$^{-1}$)	0·01 Molal α (10^3 deg.$^{-1}$)	0·10 Molal P (μv/deg.$^{-1}$)	0·10 Molal α (10^3 deg.$^{-1}$)
K	0·48	—	+358	—	+347	—
NMe_4	0·36	1·3	+287	− 3·7	+274	−3·9
NEt_4	0·29	1·7	+237	− 7·9	+229	−7·7
$N(CH_2Bu^i)_4$	0·20	2·4	+310	− 4·6	(+198 at 0·047M.)	—
$NPhMe_3$	0·31	1·5	+310 †	− 2·9	+253 †	−5·7
1-Ethylpyridinium	0·34	1·4	+314	− 2·4	+264	−4·6
1-Ethylquinolinium	0·25	1·9	+303	− 4·2	+245	−7·8
K *	0·48	—	+382	—	—	—
NMe_4 *	0·34	1·4	+310	− 4·1	—	—
NEt_4 *	0·26	1·8	+283	− 7·4	—	—
NPr^n_4 *	0·19	2·5	+279	−10·5	—	—
NBu^n_4 *	0·16	3·0	+280	−12·3	—	—
$N(CH_2Bu^n)_4$ *	0·14	3·4	+281	−13·7	—	—

* From ref. 1; thermoelectric measurements between 20° and 30°.
† These results are less certain than the rest because of experimental difficulties.

TABLE 2. *Approximate Soret coefficients, $m^{-1}(dm/dT_{stat.})$ of quaternary ammonium salts in aqueous solution.*

Salt	T_m	Calc. from data in Table 1: 0·01 molal (10^{-3} deg.$^{-1}$)	Calc. from data in Table 1: 0·10 molal (10^{-3} deg.$^{-1}$)	Directly by Tanner's method (10^{-3} deg.$^{-1}$) at T_m 30° (molality in parentheses)
NMe_4Br	29·5°	− 6	− 6	−6·5 (2·5m)
	25	− 6	—	−4·6 (1·13m)
NEt_4Br	29·5	−10	−10	—
	25	−10	—	−8·7 (1·80m)
$N(CH_2Bu^i)_4Br$	29·5	− 8	—	?0 for iodide and chloride
$NPhMe_2Br$	29·5	− 5	− 8	−7·0 (0·53m)
1-Ethylpyridinium bromide	29·5	− 5	− 7	∼−5·5 (2·01m)
1-Ethylquinolinium bromide	29·5	− 7	−11	∼−12 for iodide (0·52m)
$N(CH_2Bu^n)_4Br$	25	−19	—	—

salts (Table 2). These are compared with directly measured values, uncorrected for deviations from ideality, obtained from the preceding paper.

In view of the high and varied concentrations at which the direct measurements were done, and the fact that the values have not been corrected for deviations from ideality, the agreement is astonishingly good. It certainly proves that there is no evidence for the belief that any of the quaternary ammonium salts in aqueous solution examined have Soret coefficients close to zero. The sole exceptions to this were solutions of tetra*iso*pentylammonium chloride and iodide. These salts are not very soluble in water and are not therefore suited to examination by the Tanner method. In neither case did the experiments proceed normally, and the apparently zero value for the Soret coefficient is very doubtful, especially in view of the thermoelectric evidence. A further confirmation of the large negative Soret coefficient of tetraethylammonium bromide has recently been obtained: a conductometric determination [12] in 0·01 molal solution at a mean temperature of 25° gave $-6{\cdot}15 \times 10^{-3}$ deg.$^{-1}$.

There seems no reasonable doubt that the table of ionic entropies of transfer suggested by Goodrich *et al.*[1] is unsatisfactory, at least as far as the bromide series is concerned. This can be attributed to the very scanty experimental evidence for the conclusion that the heats (or entropies) of transfer of large symmetrical tetra-alkylammonium ions tend to a

constant value. They wrote, using the sign convention that the heated electrode is positive,

$$-\boldsymbol{F} \cdot \mathrm{d}\phi/\mathrm{d}T = (S_+^* + S_-^*)t_+ + (\Delta S_R - S_-^*)$$

where ΔS_R was the entropy change in the electrode reaction. Their experimental results are displayed in Fig. 4 of their paper, and it is claimed that the points for tetra-*n*-propyl, -butyl, and -pentyl salts lie on a straight line. These could, with as much justification, be said to be near the crest of a curve. The claim is rather more convincing for the hydroxide series, and, in fact, Soret coefficients calculated for hydroxides from these data are reasonably satisfactory in a semiquantitative way. This simply means that the table of ionic entropies for the hydroxide series in ref. (1) is probably roughly correct as a *conventional* scale with an arbitrary choice of $S_+^* = 0$ for a large tetra-alkylammonium ion. The agreement found between the ionic entropies of transfer of cations calculated from the independent experiments on bromides and hydroxides can hardly be more than fortuitous.

It is our opinion that no significance should be attached to any of the tables of heats or entropies of transfer of individual ions which have hitherto been published. There seems to be no reason why a satisfactory table, with a conventional zero, should not be constructed when sufficient accurate experimental results on Soret coefficients, especially in dilute solution, are available. Such a table must of course be consistent with the experimental measurements on thermocells.

THE UNIVERSITY, SHEFFIELD. [*Received, October 25th,* 1956.]

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411. *Pteridines. Part IV.* Derivatives of 2 : 4-Diaminopteridine and Related Compounds.*

By W. R. BOON.

A series of derivatives of 2 : 4-diaminopteridine having one or both amino-groups substituted, has been prepared by condensation of the appropriate tetra-aminopyrimidines and α-diketones. Substances with different substituents in positions 6 and 7 have been prepared from 5-arylazo-6-(α-pyrimidylamino)-ketones. Recorded preparations of disubstituted aminopteridines from aminohydroxy- and aminomercapto-pteridines are, in some cases, shown to be erroneous.

The coupling of pyrimidine derivatives with aryldiazonium salts is shown to be a reaction more widely applicable than is generally known.

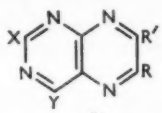
SEVERAL derivatives of 2 : 4-diaminopteridine are known to possess antimalarial activity (for a summary see Potter and Henshall [1]). It was considered of interest to prepare a series of related derivatives of 2 : 4-diamino-6 : 7-diphenylpteridine (I; X = Y = NH_2, R = R′ = Ph) in which the primary amino-groups were progressively substituted by methyl. Antimalarial activity was immediately lost, but the compounds were active against experimental schistosomiasis in mice. Further modifications of the substituents X, Y, R, and R′ always lowered the activity. The only other substances examined showing appreciable activity were those in which X = Y = NHMe, R = R′ = *p*-MeO·C_6H_4 and *m*- or *p*-C_6H_4Cl.

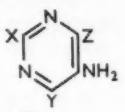
Substances (I) in which R = R′ are most conveniently prepared by condensing a tetra-aminopyrimidine with an α-diketone, the 2- and 4-amino-groups being substituted as required. The tetra-aminopyrimidines are obtained by reducing a substance (II) in which X and Y are amino- or substituted amino-groups and Z is, *e.g.*, arylazo, nitro or nitroso.

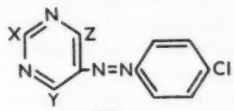
* Part III, *J.*, 1951, 1497.

[1] Potter and Henshall, *J.*, 1956, 2000.

4 : 5 : 6-Triamino-2-dimethylaminopyrimidine was the only known substance required [2,3] but the methods by which it was obtained are not suitable for the preparation of compounds where the 4-amino-group also is substituted.


(I)


(II)


(III)

For the preparation of 2-dimethylamino-derivatives, 2-dimethylamino-4 : 6-dihydroxy-5-nitropyrimidine was readily obtained by nitration of 2-dimethylamino-4 : 6-dihydroxypyrimidine,[4] but, although it readily gave the 4 : 6-dichloro-compound, stepwise replacement of the chlorine atoms by amino-groups proved difficult, so that approach was abandoned.

When a 2-amino-group was required, 2 : 6-diamino-4-chloro-5-*p*-chlorophenylazopyrimidine proved a convenient starting material.[5] 2-Amino-4-chloro-5-*p*-chlorophenylazo-6-methylamino- and 4-amino-6-chloro-5-*p*-chlorophenylazo-2-methylamino-pyrimidine were also readily obtained. Lythgoe, Todd, and Topham [6] state that only those pyrimidine compounds which contain tautomerisable hydrogen atoms on at least two of the substituents in positions 2, 4, and 6 can be caused to couple with diazonium salts. Polonovski and Pesson,[7] however, state that for coupling to occur with a 4-amino- or 4-hydroxy-pyrimidine there must be a second polar group in position 2; they describe, *inter alia*, the coupling, in alkaline solution, of 2-dimethylamino-4-hydroxy-6-methylpyrimidine with benzenediazonium chloride. This procedure has now been used for the preparation of 4-chloro-5-*p*-chlorophenylazo-2-dimethylamino-6-hydroxypyrimidine (III; X = NMe_2, Y = Cl, Z = OH) and the corresponding 2-methylamino-compound. On the other hand, coupling of 4-amino-6-chloro-2-dimethylamino- and 2-amino-4-chloro-6-dimethylamino-pyrimidine with *p*-chlorobenzenediazonium chloride occurred most readily under mildly acid conditions, giving the 5-*p*-chlorophenylazo-compounds. Coupling was also satisfactory with a number of other diazonium salts (see Table 1 and B.P. 763,041). 4-Chloro-5-*p*-chlorophenylazo-2 : 6-bisdimethylaminopyrimidine and 5-*p*-chlorophenylazo-2-dimethylamino-4-hydroxy-6-methylpyrimidine were obtained similarly.

The 4-chlorine was readily replaced when 2 : 6-diamino-5-arylazopyrimidines were heated with ammonia or an amine. In preliminary experiments, because of the low solubility of the starting materials in more conventional solvents, dimethylformamide was used as an additional solvent in reaction with alcoholic ammonia, but the ammonia then reacted preferentially with the amide so that the chlorine atom was replaced by a dimethylamino-group; thus, the compounds (III; X = NHMe, Y = NH_2, Z = Cl; X = Y = NHMe, Z = Cl; X = NH_2, Y = NHMe, Z = Cl) gave the products in which Z = NMe_2, identical with those obtained by the direct action of alcoholic dimethylamine on the starting materials.

Reduction of the azo-compounds by hydrogen in presence of Raney nickel was smooth in every case. Condensation of the products with symmetrical α-diketones proceeded as expected. The amine (II; X = Z = NH_2, Y = NHMe) with benzil gave 2-amino-4-methylamino-6 : 7-diphenylpteridine (I; X = NH_2, Y = NHMe, R = R′ = Ph), m. p. 272°, which Paget [8] has shown to be preferentially absorbed on cardiac muscle. Cain, Taylor, and Daniel [9] state that this substance has m. p. 237—238°; they heated under reflux a mixture of 2-amino-4-hydroxy-6 : 7-diphenylpteridine, phosphorus oxychloride, and

[2] Roth, Smith, and Hultquist, *J. Amer. Chem. Soc.*, 1951, **73**, 2864.
[3] Andrews, Anand, Todd, and Topham, *J.*, 1949, 2490.
[4] Boon, *J.*, 1952, 1532.
[5] B.P. 677,342.
[6] Lythgoe, Todd, and Topham, *J.*, 1944, 315.
[7] Polonovski and Pesson, *Bull. Soc. chim. France*, 1948, **15**, 688.
[8] Paget, *J. Path. Bact.*, in the press.
[9] Cain, Taylor, and Daniel, *J. Amer. Chem. Soc.*, 1949, **71**, 892.

phosphorus pentachloride and heated the crude product at 150° with alcoholic methylamine; repetition of this work gave a product of m. p. 253—259°, depressed on admixture with a sample prepared as above, and shown by fractional extraction with acid to be a mixture of 2 : 4-bismethylamino-6 : 7-diphenylpteridine (I; X = Y = NHMe, R = R′ = Ph) and the methylamide of 3-amino-5 : 6-diphenylpyrazine-2-carboxylic acid. However, reaction with alcoholic methylamine at <120° gave the expected 2-amino-4-methylamino-6 : 7-diphenylpteridine.

Likewise 4-amino-2-methylamino-6 : 7-diphenylpteridine (I; X = NHMe, Y = NH_2, R = R′ = Ph) obtained from (II; X = NHMe, Y = Z = NH_2) and benzil had m. p. 307° although Taylor and Cain [10] state that the substance obtained from the action of methylamine on 4-amino-2-mercapto-6 : 7-diphenylpteridine (I; X = SH, Y = NH_2, R = R′ = Ph) has m. p. 264—265°. Repetition showed that their substance was 2 : 4-bismethylamino-6 : 7-diphenylpteridine. Further, the product, m. p. 192—195°, described by these authors as (I; X = Me_2N, Y = NH_2, R = R′ = Ph) is a mixture of this substance which has m. p. 239° and (I; X = Y = NMe_2, R = R′ = Ph), m. p. 210°, both of which have been prepared by unambiguous methods during the present work.

For the preparation of substances containing only one substituent at position 6 or 7, or with different substituents in these positions, reductive cyclisation of an α-(5-arylazo-4-pyrimidylamino)-ketone appeared the most satisfactory unambiguous method. The condensation of (III; X = Y = NH_2, Z = Cl) with glycine ethyl ester has already been recorded.[5] Analogous condensations were slower as the amino-groups were progressively substituted, and still slower when the second reactant was an α-amino-ketone so that the use of a protected derivative such as a semicarbazone or acetal was essential. In contrast, a 4-hydroxyl group increased the reactivity of the 6-chlorine atom, so that the hydroxy-compound (III; X = NMe_2, Y = OH, Z = Cl) condensed more readily than the primary diamine (III; X = Y = NH_2, Z = Cl). 4-Chloro-5-*p*-chlorophenylazo-2-dimethylamino-6-hydroxypyrimidine (III; X = NMe_2, Y = OH, Z = Cl) with ω-aminoacetophenone semicarbazone and α-amino-α-phenylacetaldehyde dimethyl acetal gave products which on hydrolysis afforded the ketone and aldehyde (III; X = NMe_2, Y = OH, Z = NH·CH_2·COPh and NH·CHPh·CHO). These were reduced to 2-dimethylamino-7 : 8-dihydro-4-hydroxy-6- and -7-phenylpteridines (IV; R = Ph, R′ = H; R = H, R′ = Ph) respectively which were oxidised to the pteridines with alkaline permanganate. The last two compounds were also obtained by condensing 4 : 5-diamino-2-dimethylamino-6-hydroxypyrimidine with phenylglyoxal at pH 1 (6-phenyl compound) or 4 (7-phenyl compound). In the latter case, 4-amino-2-dimethylamino-6-hydroxy-5-phenacylideneaminopyrimidine (II; X = NMe_2, Y = OH, Z = N:CH·COPh) was first obtained and then cyclised to the pteridine by heating it with sodium hydroxide.

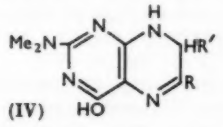
The 6- and the 7-phenyl compound were converted into the 2 : 4-bisdimethylaminopteridines (III; X = Y = NMe_2, R = Ph, R′ = H; X = Y = NMe_2, R = H, R′ = Ph) by phosphorus oxychloride under reflux, the crude chloro-compounds being treated with alcoholic dimethylamine. From the 6-phenylpteridine some 4-ethoxy-compound (I; X = NMe_2, Y = EtO, R = Ph, R′ = H) was obtained also. The same bisdimethylaminopteridines were obtained by condensing 4 : 5-diamino-2 : 6-bisdimethylaminopyrimidine (II; X = Y = NMe_2, Z = NH_2) with phenylglyoxal under the conditions used for the corresponding hydroxy-compounds; in this case though, the intermediate substance corresponding to the 7-phenyl compound was not isolated. As a further check on the identity of the products both 2 : 4-bisdimethylamino-compounds were converted into the corresponding 2-dimethylamino-4-hydroxy-compounds by hydrolysis with hydrochloric acid.

Although this series of transformations showed that condensation of phenylglyoxal could be directed to give predominantly one or the other of the two possible pteridines, it was considered unlikely that this would be possible with an α-diketone in which there is a

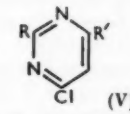
[10] Taylor and Cain, *J. Amer. Chem. Soc.*, 1952, **74**, 1644.

smaller difference in the reactivity of the keto-groups. The stepwise synthesis of such pteridines appeared essential in these cases.

Although both 4 : 6-dichloro-2-methylamino- and -2-dimethylamino-pyrimidine condensed smoothly with glycine ethyl ester to give the amines (V; R = NHMe or NMe_2, R′ = $NH{\cdot}CH_2{\cdot}CO_2Et$), no satisfactory products could be obtained with α-aminodeoxybenzoin.



(IV)



(V)

Because of the greater reactivity of the chlorine atoms in trichloropyrimidine, reaction of this substance with an α-amino-ketone appeared to offer a suitable starting point provided the two products could be separated. Trichloropyrimidine with ω-amino-ω-*p*-chlorophenylacetophenone gave a mixture which could not readily be separated but with alcoholic dimethylamine gave a readily separable mixture of amines (V; R = NMe_2, R′ = *p*-$C_6H_4Cl{\cdot}CHBz{\cdot}NH$ and *vice versa*). The subsequent stages in the conversion of the former into the diamine (I; X = Y = NMe_2, R = Ph, R′ = *p*-C_6H_4Cl) proceeded smoothly. In the reaction between trichloropyrimidine and aminodeoxybenzoin, the product (V; R = Cl, R′ = $Ph{\cdot}CHBz{\cdot}NH$) separated directly from the reaction mixture.

Experimental

2-Dimethylamino-4 : 6-dihydroxy-5-nitropyrimidine.—2-Dimethylamino-4 : 6-dihydroxypyrimidine (70 g.),[4] ground to pass a 30-mesh sieve, was added with stirring during 45 min. to a mixture of glacial acetic acid (280 c.c.) and nitric acid (*d* 1·5; 65 c.c.) at 20—25°. After a further 45 minutes' stirring the mixture was poured into water (1350 c.c.). The solid was separated, washed free from acid, and dried (81 g.). No suitable solvent could be found for crystallisation and the *nitro-compound* was analysed directly (Found: C, 36·1; H, 4·4; N, 27·7. $C_6H_8O_4N_4$ requires C, 36·0; H, 4·0; N, 28·0%).

4 : 6-Dichloro-2-dimethylamino-5-nitropyrimidine.—2-Dimethylamino-4 : 6-dihydroxy-5-nitropyrimidine (20 g.), phosphorus oxychloride (60 c.c.), and dimethylaniline (20 c.c.) were heated to 105° (bath-temperature) whereupon a vigorous reaction set in. When this had moderated heating was continued for 1 hr. After removal of the excess of phosphorus oxychloride under reduced pressure the residue was treated with ice (200 g.), then the suspension was extracted with ether (4 × 50 c.c.). The extract was dried ($MgSO_4$), filtered, and evaporated. The residue, crystallised from light petroleum (b. p. 60—80°) (yield, 3·7 g.), had m. p. 117—120°. The *compound* was purified for analysis by sublimation at 150°/19 mm. (Found: C, 30·6; H, 2·5; N, 23·6; Cl, 29·9. $C_6H_6O_2N_4Cl_2$ requires C, 30·4; H, 2·5; N, 23·6; Cl, 29·9%).

4-Amino-6-chloro-2-dimethylamino-5-nitropyrimidine and 4 : 6-Diamino-2-dimethylamino-5-nitropyrimidine.—4 : 6-Dichloro-2-dimethylamino-5-nitropyrimidine (14 g.), benzene (90 c.c.), and ammonia (*d* 0·880) (10 c.c.) were shaken overnight and filtered. The residue of the *diamine* (4·2 g.), after two crystallisations from dioxan, had m. p. 249—250° (Found: C, 36·6; H, 5·1; N, 42·5. $C_6H_{10}O_2N_6$ requires C, 36·6; H, 5·2; N, 42·75%). Evaporation of the filtrate gave a residue of indefinite m. p. from which the *monoamino-compound* (0·5 g.) was obtained by chromatography on alumina (120 g.) in benzene (30 c.c.) and crystallisation from ethyl acetate–light petroleum (b. p. 60—80°) and had m. p. 132° (Found: C, 33·0; H, 3·9; N, 32·6; Cl, 15·9. $C_6H_8O_2N_5Cl$ requires C, 33·1; H, 3·7; N, 32·2; Cl, 16·4%).

4 : 6-Dihydroxy-2-methylaminopyrimidine.—To a solution of sodium (91 g.) in methanol (2 l.) methylguanidine sulphate (509 g.) was added and the mixture heated under reflux for 30 min. with stirring. Ethyl malonate was then added and heating was continued for 6 hr. After cooling, the mixture was diluted with water (5 l.), treated with carbon, and filtered. Acidification to litmus with acetic acid precipitated the dihydroxypyrimidine (183 g.) immediately. After this had been collected the mother-liquors deposited a second product (15 g.), presumably *2-amino-1 : 4 : 5 : 6-tetrahydro-1-methyl-4 : 6-dioxopyrimidine*, m. p. >360°, purified for analysis by dissolution in aqueous sodium hydroxide, treatment with charcoal, and reprecipitation with acetic acid (Found: C, 42·3; H, 5·3; N, 28·7. $C_5H_7O_2N_3$ requires C, 42·5; H, 5·0; N, 29·8%).

4 : 6-Dichloro-2-methylaminopyrimidine.—4 : 6-Dihydroxy-2-methylaminopyrimidine (93 g.)

XUM

and phosphorus oxychloride (510 c.c.) were heated under reflux for 1 hr. After filtration through sintered-glass the solution was poured on 32% aqueous sodium hydroxide (2250 c.c.) and ice. The solid which separated was washed with water and crystallised from methanol. The product (88 g.) had m. p. 164° undepressed on admixture with an authentic sample.[11]

4-Chloro-6-methoxy-2-methylaminopyrimidine.—4 : 6-Dichloro-2-methylaminopyrimidine (130 g.) was heated in a solution of sodium (168 g.) in methanol (570 c.c.) for 12 hr. The *ether* which separated on cooling was collected, washed with water, and crystallised from methanol; it (95 g.) had m. p. 153° (Found: C, 41·8; H, 4·7; N, 24·2; Cl, 20·3. $C_6H_8ON_3Cl$ requires C, 41·5; H, 4·6; N, 24·2; Cl, 20·5%).

4-Chloro-2-dimethylamino-6-methoxypyrimidine, m. p. 62° after sublimation (55°/0·1 mm.), was obtained similarly (81%) from 4 : 6-dichloro-2-dimethylaminopyrimidine at room temperature (Found: C, 44·7; H, 5·4; N, 22·5; Cl, 19·2. $C_7H_{10}ON_3Cl$ requires C, 44·8; H, 5·3; N, 22·4; Cl, 18·9%).

4-Chloro-6-hydroxy-2-methylaminopyrimidine.—4-Chloro-6-methoxy-2-methylaminopyrimidine (10 g.) was heated on the steam-bath for 30 min. with concentrated hydrochloric acid (50 c.c.). The *hydroxy-compound* which separated on cooling was collected and purified by dissolution in alkali, etc., as above, and had m. p. 265° (decomp.) (5·5 g.) (Found: C, 38·3; H, 4·1; N, 26·2. $C_5H_6ON_3Cl$ requires C, 37·6; H, 3·8; N, 26·3%).

4-Chloro-2-dimethylamino-6-hydroxypyrimidine, m. p. 217°, was obtained similarly (95%) from 4-chloro-2-dimethylamino-6-methoxypyrimidine (Found: C, 41·9; H, 4·9; N, 23·9; Cl, 21·0. $C_6H_8ON_3Cl$ requires C, 41·5; H, 4·6; N, 24·2; Cl, 20·5%).

2-Amino-4-dimethylamino-6-methylpyrimidine.—2-Amino-4-chloro-6-methylpyrimidine (28·7 g.) and dimethylamine (78 c.c. of a 19·5% w/v solution in ethanol) were heated at 110—120° for 17 hr. The diamine, crystallised from benzene, had m. p. 172° (165 g.) (Found: C, 55·8; H, 8·4; N, 37·1. $C_7H_{12}N_4$ requires C, 55·3; H, 7·9; N, 36·8%).

α-(2 : 4-Dichloro-6-pyrimidylamino)deoxybenzoin.—α-Aminodeoxybenzoin hydrochloride (47 g.), dissolved in water (750 c.c.), was basified with ammonia at 0°. The precipitated base was collected, drained as dry as possible, added to trichloropyrimidine (35 g.) in ethanol (750 c.c.) and set aside at room temperature for 2 days. The *ketone* (12 g.) was collected and crystallised from ethanol; it had m. p. 165° (Found: C, 60·1; H, 3·8; N, 11·8; Cl, 19·9. $C_{18}H_{13}ON_3Cl_2$ requires C, 60·4; H, 3·6; N, 11·7; Cl, 19·85%).

ω-(4-Chloro-2-dimethylamino-6-pyrimidylamino)-ω-p-chlorophenylacetophenone and ω-(4-Chloro-6-dimethylamino-2-pyrimidylamino)-ω-p-chlorophenylacetophenone.—ω-Amino-ω-*p*-chlorophenylacetophenone hydrochloride (28·5 g.) was converted into the base and caused to react with trichloropyrimidine (9 g.) under the conditions given above. The crude product which could not be purified readily was heated under reflux for 3 hr. with dimethylamine in ethanol (10 c.c. of 19·5% w/v solution) and ethanol (10 c.c.). On evaporation of the solution to half its volume a solid, m. p. 75—95°, was obtained. Crystallisation and recrystallisation from methanol gave the *2-dimethylaminopyrimidine*, m. p. 151—152° (Found: C, 60·3; H, 4·8; N, 13·9; Cl, 17·5. $C_{20}H_{18}ON_4Cl_2$ requires C, 59·8; H, 4·5; N, 13·9; Cl, 17·7%). The *6-dimethylaminopyrimidine*, m. p. 181—182° (Found: C, 60·1; H, 4·7; N, 14·0%), was obtained by concentration of the mother-liquors and recrystallisation from ethanol. A small quantity of another substance, m. p. 239—240°, believed to be 2 : 5-di-*p*-chlorophenyl-3 : 6-diphenylpyrazine, was also obtained.

Derivatives of 2 : 4-Diamino-6-chloropyrimidine.—(a) *From 2-amino(or substituted amino)-4 : 6-dichloropyrimidine. 2-Amino-4-chloro-6-dimethylaminopyrimidine.* 2-Amino-4 : 6-dichloropyrimidine (33 g.) was heated with dimethylamine in ethanol (175 c.c. of 19·5% w/v solution) for 3 hr. after the initial reaction had subsided. The *diamino-compound* (24 g.) which separated on cooling was collected, crystallised from methanol and then from benzene, and had m. p. 164—165° (Found: C, 41·9; H, 5·0; N, 32·5; Cl, 20·8. $C_6H_9N_4Cl$ requires C, 41·7; H, 5·2; N, 32·5; Cl, 20·5%).

The following were obtained similarly (in 70% yield) from the appropriate derivative of 2-amino-4 : 6-dichloropyrimidine and an ethanol solution of glycine ethyl ester:

Ethyl 4-chloro-2-methylamino-6-pyrimidylaminoacetate, m. p. 167° (Found: C, 43·6; H, 4·9; N, 22·8; Cl, 14·7. $C_9H_{13}O_2N_4Cl$ requires C, 44·2; H, 5·3; N, 22·9; Cl, 14·5%).

Ethyl 4-chloro-2-dimethylamino-6-pyrimidylaminoacetate, m. p. 121° (Found: C, 46·5; H, 5·6; N, 21·0; Cl, 14·2. $C_{10}H_{15}O_2N_4Cl$ requires C, 46·4; H, 5·8; N, 21·6; Cl, 13·7%).

[11] Winkelmann, *J. prakt. Chem.*, 1927, **115**, 292.

(b) *From* 2 : 4-*dichloro*-6-*methylaminopyrimidine.* 4-*Chloro*-2-*ethylamino*-6-*methylaminopyrimidine.* 2 : 4-Dichloro-6-methylaminopyrimidine (36 g.), ethanol (200 c.c.), and aqueous ethylamine (50 g. of 70% w/w solution) were heated under reflux for 6 hr. After removal of the ethanol the mixture was diluted with water and extracted with ether. After drying, the ether was removed and the residue was dissolved in absolute ethanol (70 c.c.). Concentrated sulphuric acid (9 c.c.) was added until the mixture was acid to Congo-red; dry ether was then added to produce a permanent turbidity, the *diamine sulphate* separating (34 g.). After recrystallisation from ethanol–ether it had m. p. 148° (Found : C, 29·9; H, 5·0; N, 19·4; Cl, 12·5; S, 11·2. $C_7H_{11}N_4Cl,H_2SO_4$ requires C, 29·5; H, 4·6; N, 19·7; Cl, 12·45; S, 11·25%).

The following were obtained similarly : 4-*chloro*-2-*dimethylamino*-6-*methylaminopyrimidine*, m. p. 78° (from light petroleum) (Found : C, 45·5; H, 6·2; N, 30·6; Cl, 19·0. $C_7H_{11}N_4Cl$ requires C, 45·1; H, 5·9; N, 30·0; Cl, 19·0%); 4-*chloro*-2-*diethylamino*-6-*methylaminopyrimidine sulphate*, m. p. 148—149° (from ethanol–ether) (Found : C, 34·5; H, 5·6; N, 18·1; Cl, 11·6; S, 10·1. $C_9H_{15}N_4Cl,H_2SO_4$ requires C, 34·6; H, 5·4; N, 17·9; Cl, 11·4; S, 10·2%); 4-*chloro*-6-*methylamino*-2-*piperidinopyrimidine*, m. p. 118° (from methanol) (Found : C, 53·3; H, 6·8; N, 24·1; Cl, 15·5. $C_{10}H_{15}N_4Cl$ requires C, 53·0; H, 6·6; N, 24·7; Cl, 15·7%); 4-*chloro*-2-2′-*dimethylaminoethylamino*-6-*methylaminopyrimidine*, m. p. 99° (from ethyl acetate–light petroleum) (Found : C, 47·1; H, 6·9; N, 29·6; Cl, 15·5. $C_9H_{16}N_5Cl$ requires C, 47·1; H, 6·9; N, 30·5; Cl, 15·5%).

4-*Chloro*-5-p-*chlorophenylazo*-2-*dimethylamino*-6-*hydroxypyrimidine.*—To a solution of 4-chloro-2-dimethylamino-6-hydroxypyrimidine (17·5 g.) dissolved in water (500 c.c.) containing 2N-sodium hydroxide (60 c.c.) and sodium hydrogen carbonate (12·6 g.), a solution of *p*-chlorobenzenediazonium chloride (from 12·75 g. of *p*-chloroaniline) was added. After overnight stirring the *azo-compound* was collected, washed with water, ethanol, and ether, and crystallised from dioxan; it had m. p. 220—222° (decomp.) (20 g.) (Found : C, 46·4; H, 3·5; N, 22·7; Cl, 22·6. $C_{12}H_{11}ON_5Cl_2$ requires C, 46·2; H, 3·5; N, 22·5; Cl, 22·8%). 4-Chloro-5-*p*-chlorophenylazo-6-hydroxy-2-methylaminopyrimidine was obtained similarly but could not be purified without decomposition. The washed crude material was satisfactory for further use.

5-p-*Chlorophenylazo*-2-*dimethylamino*-4-*hydroxy*-6-*methylpyrimidine.*—M/40-*p*-Chlorobenzenediazonium chloride solution (500 c.c.) and crystalline sodium acetate (46 g.) were added with stirring to a solution of 2-dimethylamino-4-hydroxy-6-methylpyrimidine (3·8 g.) in water (500 c.c.). After 16 hr. the *azo-compound* was collected, washed, dried in air, and recrystallised from butanol, then having m. p. 216—217° (5·5 g.) (Found : C, 53·4; H, 4·7; N, 24·2. $C_{13}H_{14}ON_5Cl$ requires C, 53·5; H, 4·8; N, 24·1%).

2 : 6-*Diamino*-5-*arylazo*-4-*chloropyrimidines.*—The preparation of 4-*chloro*-5-p-*chlorophenylazo*-2 : 6-*bisdimethylaminopyrimidine* is typical. M/40-*p*-Chlorophenyldiazonium chloride (50 c.c.) and crystalline sodium acetate (40 g.) were added with stirring to a solution of 4-chloro-2 : 6-bisdimethylaminopyrimidine (5·0 g.) in acetic acid (70 c.c.) diluted with water (200 c.c.). The dark red oil which separated changed to a granular solid after 48 hours' stirring. The azo-compound was then collected, washed with water, and crystallised twice from ethanol; it (5 g.) had m. p. 91° (Found : C, 49·7; H, 4·6; N, 24·7; Cl, 20·9. $C_{14}H_{16}N_6Cl_2$ requires C, 49·6; H, 4·7; N, 24·8; Cl, 20·9%). Details of other compounds in this series are given in Table 1 and in B.P. 763,041.

2 : 4 : 6-*Triamino*-5-*arylazopyrimidine Derivatives.*—The preparation of 4 : 6-*diamino*-5-p-*chlorophenylazo*-2-*dimethylaminopyrimidine* is typical. 4-Amino-6-chloro-5-*p*-chlorophenylazo-2-dimethylaminopyrimidine (2 g.) and saturated alcoholic ammonia (40 c.c.) were heated at 150—160° for 36 hr. The triamino-compound (1·75 g.) which separated on cooling was crystallised from butanol; it had m. p. 272—273° (Found : C, 49·1; H, 4·8; Cl, 12·2. $C_{12}H_{14}N_7Cl$ requires C, 49·4; H, 4·8; Cl, 12·2%). The *hydrochloride* was obtained as follows : *p*-chlorobenzenediazonium chloride [from *p*-chloroaniline (6·5 g.), water (60 c.c.), concentrated hydrochloric acid (11 c.c.), and sodium nitrite (3·5 g.)] was added with stirring to 4 : 6-diamino-2-dimethylaminopyrimidine (7·5 g.) in glacial acetic acid (70 c.c.). The product separated rapidly and sufficient 50% acetic acid was added to keep the mixture mobile. The hydrochloride (14·1 g.) was collected after 4 hr., washed with water and ethanol; it had m. p. 301° (decomp.) when crystallised from 80% formic acid (Found : C, 44·6; H, 4·4; N, 29·9; Cl, 21·6. $C_{12}H_{14}N_7Cl,HCl$ requires C, 44·0; H, 4·6; N, 29·9; Cl, 21·5%). The free base identical with the above was obtained by trituration with ammonia.

Table 2 gives details of substances containing an unsubstituted 4-amino-group prepared by

reaction of the corresponding 4-chloro-compounds (I) with ammonia or the appropriate amine. Further examples are given in B.P. 763,042.

5-p-*Chlorophenylazo*-4-*dimethylamino*-2 : 6-*bismethylaminopyrimidine*.—4-Chloro-5-*p*-chlorophenylazo-2 : 4-bismethylaminopyrimidine (5 g.), dimethylformamide (100 c.c.), and 10% ethanolic ammonia (20 c.c.) were heated at 60° for 64 hr. The *amine* which separated on addition of water crystallised from ethanol and had m. p. 145° (4 g.) (Found: C, 52·4; H, 5·5. $C_{14}H_{18}N_7Cl$ requires C, 52·6; H, 5·5%). The same product (m. p. and mixed m. p.) was obtained by reaction between 4-chloro-5-*p*-chlorophenylazo-2 : 6-bismethylaminopyrimidine and methanolic dimethylamine under standard conditions.

2-*Amino*-5-p-*chlorophenylazo*-4-*dimethylamino*-6-*methylaminopyrimidine*, m. p. 192° (Found: C, 51·4; H, 5·5. $C_{13}H_{16}N_7Cl$ requires C, 51·1; H, 5·2%), was obtained by reaction between 2-amino-4-chloro-5-*p*-chlorophenylazo-6-methylaminopyrimidine and alcoholic ammonia in dimethylformamide.

5-p-*Chlorophenylazo*-2 : 4 : 6-*trismethylaminopyrimidine*, m. p. 155° (Found: C, 51·4; H, 5·3; N, 31·3; Cl, 11·6. $C_{13}H_{16}N_7Cl$ requires C, 51·1; H, 5·3; N, 31·1; Cl, 11·6%), was obtained from 4-chloro-5-*p*-chlorophenylazo-2 : 6-bismethylaminopyrimidine and methylamine in dimethylformamide.

Tetra-aminopyrimidines.—The following procedure for the preparation of 2 : 4 : 5-*triamino*-4-*methylaminopyrimidine* is typical: 2 : 4-Diamino-5-*p*-chlorophenylazo-6-methylaminopyrimidine (5 g.) in ethanol (75 c.c.) was reduced by hydrogen in presence of Raney nickel (initial pressure 47 atm.) at 90—95° for 5 hr. The mixture was then acidified with acetic acid (4 c.c.) and filtered through Hyflo Supercel, and the residue washed with water. The combined filtrate and washings were evaporated to dryness under reduced pressure in an atmosphere of nitrogen. The brown residue was triturated with ether, filtered, washed with more ether to remove *p*-chloroaniline, dissolved in water (10 c.c.), and acidified to Congo-red with sulphuric acid. The *sulphate* was precipitated by addition of ethanol and crystallised from water.

No satisfactory analytical results could be obtained for 2 : 5-diamino-6-diethylamino-4-dimethylaminopyrimidine oxalate, m. p. 221° (decomp.), although it condensed normally with benzil to give the corresponding diphenylpteridine.

Details of other compounds prepared by this method are given in Table 3 and in B.P. 763,120.

5-*Arylazopyrimidylamino-aldehydes and -ketones and Derivatives*.—5-p-*Chlorophenylazo*-2-*dimethylamino*-4-*methylamino*-6-*pyrimidylaminoacetaldehyde diethyl acetal*. Aminoacetaldehyde diethyl acetal (15 g.) and 4-chloro-5-*p*-chlorophenylazo-2-dimethylamino-4-methylaminopyrimidine (17·5 g.) were heated under reflux for 24 hr. in dioxan (250 c.c.). The residue obtained on evaporation was triturated with ethanol and filtered. The *acetal* (10 g.), crystallised from light petroleum (b. p. 60—80°), had m. p. 95° (Found: C, 54·3; H, 6·4; N, 24·0; Cl, 8·0. $C_{19}H_{28}O_2N_7Cl$ requires C, 54·1; H, 6·7; N, 23·3; Cl, 8·4%).

α-5-p-*Chlorophenylazo*-2 : 4-*bisdimethylamino*-6-*pyrimidylamino*-α-*phenylacetaldehyde Dimethyl Acetal*.—α-Aminophenylacetaldehyde dimethyl acetal (11 g.) and 4-chloro-5-*p*-chlorophenylazo-2 : 6-bisdimethylaminopyrimidine in dioxan (250 c.c.) were heated under reflux for 4 hr. After removal of the solvent, the *acetal* (1·9 g.) was crystallised from butanol; it had m. p. 151° (Found: C, 59·5; H, 6·3; Cl, 7·7. $C_{24}H_{30}O_2N_7Cl$ requires C, 59·6; H, 6·2; Cl, 7·4%).

α-(5-p-*Chlorophenylazo*-2-*dimethylamino*-4-*hydroxy*-6-*pyrimidylamino*)-α-*phenylacetaldehyde dimethyl acetal*, m. p. 242° (from butanol), was obtained similarly from 4-chloro-5-*p*-chlorophenylazo-2-dimethylamino-6-hydroxypyrimidine (Found: C, 58·0; H, 5·6; N, 18·4; Cl, 7·8. $C_{22}H_{25}O_3N_6Cl$ requires C, 57·8; H, 5·5; N, 18·4; Cl, 7·8%).

5-p-*Chlorophenylazo*-2-*dimethylamino*-4-*hydroxy*-6-*pyrimidylaminoacetone*.—Aminoacetone semicarbazone hydrochloride (11 g.) was stirred for 2 hr. with a solution of cold sodium ethoxide (from sodium, 1·5 g., and ethanol, 60 c.c.), 4-chloro-5-*p*-chlorophenylazo-2-dimethylamino-6-hydroxypyrimidine (9·3 g.) in dimethylformamide (140 c.c.) was then added, and stirring was continued for a further 15 hr. The semicarbazone (11 g.), m. p. 243°, was collected, washed well with water and ethanol, and dissolved in glacial acetic acid (25 c.c.) and 2N-hydrochloric acid (150 c.c.). After being kept overnight the mixture was filtered and evaporated to dryness. The *hydrochloride* (6·6 g.), crystallised from ethanol, had m. p. 217° (Found: C, 46·6; H, 4·9; N, 21·3. $C_{15}H_{17}O_2N_6Cl,HCl$ requires C, 46·8; H, 4·7; N, 21·8%).

The following were obtained similarly:

ω-(5-p-*Chlorophenylazo*-2-*dimethylamino*-4-*hydroxy*-6-*pyrimidylamino*)*acetophenone hydrochloride monohydrate*, m. p. 229° (from ethanol) (Found : C, 51·4; H, 4·7; N, 18·0; Cl, 15·4. $C_{20}H_{19}O_2N_6Cl,HCl,H_2O$ requires C, 51·6; H, 4·7; N, 18·0; Cl, 15·3%); *semicarbazone*, m. p. 263° (decomp.) (from dimethylformamide–ethanol) (Found : C, 53·5; H, 4·9; N, 28·0; Cl, 7·7. $C_{21}H_{23}O_2N_9Cl$ requires C, 53·9; H, 4·7; N, 27·0; Cl, 7·6%).

4-*Chloro*-ω-(5-p-*chlorophenylazo*-4-*hydroxy*-2-*methylamino*-6-*pyrimidylamino*)*acetophenone hydrochloride*, m. p. 258° (decomp.) (Found : C, 48·8; H, 3·8; N, 17·1. $C_{19}H_{16}O_2N_6Cl_2,HCl$ requires C, 48·8; H, 3·6; N, 17·9%); *semicarbazone*, m. p. 264° (from dimethylformamide) (Found : C, 49·3; H, 3·9. $C_{20}H_{19}O_2N_9Cl_2$ requires C, 49·2; H, 3·9%).

4-*Chloro*-ω-(5-p-*chlorophenylazo*-2-*dimethylamino*-4-*hydroxy*-6-*pyrimidylamino*)*acetophenone*, m. p. 244° (decomp.) (from dimethylformamide–ethanol) (Found : C, 54·2; H, 4·0; N, 18·8; Cl, 16·0. $C_{20}H_{18}O_2N_6Cl_2$ requires C, 53·9; H, 4·0; N, 18·9; Cl, 16·0%); *semicarbazone*, m. p. 255° (decomp.) (from dimethylformamide–ethanol) (Found : C, 50·7; H, 4·3; N, 24·7; Cl, 14·6. $C_{21}H_{21}O_2N_9Cl_2$ requires C, 50·2; H, 4·2; N, 25·1; Cl, 14·1%).

α-(4-*Chloro*-5-p-*chlorophenylazo*-2-*dimethylamino*-6-*pyrimidylamino*)*deoxybenzoin*.—α-(2 : 4-Dichloro-6-pyrimidylamino)deoxybenzoin (17·5 g.) and 2·5M-ethanolic dimethylamine (60 c.c.) were heated under reflux for 3 hr., and the solid which separated on cooling (17 g. ; m. p. 178—183°) was collected and dissolved in acetic acid (200 c.c.) together with crystalline sodium acetate (19 g.). To this solution *p*-chlorobenzenediazonium chloride [from *p*-chloroaniline (6 g.), sodium nitrate (3·4 g.), concentrated hydrochloric acid (10 c.c.), and water (34 c.c.)] was added. After four days' stirring the *azo-compound* was collected, washed with water and ethanol, and crystallised from butanol, then having m. p. 254° (decomp.) (10 g.) (Found : C, 61·8; H, 4·1; N, 16·9; Cl, 14·5. $C_{26}H_{22}ON_6Cl_2$ requires C, 61·8; H, 4·4; N, 16·7; Cl, 14·1%).

α-(5-p-*Chlorophenylazo*-2 : 4-*bisdimethylamino*-6-*pyrimidylamino*)*deoxybenzoin*.—The above chloropyrimidine (10 g.) was heated under reflux for 20 hr. with 2·5M-ethanolic dimethylamine (340 c.c.). The *diamino-compound* (5·5 g.) which separated on cooling crystallised from ethanol and had m. p. 179° (Found : C, 65·7; H, 5·4; N, 19·2; Cl, 7·4. $C_{28}H_{28}ON_7Cl$ requires C, 65·4; H, 5·5; N, 19·1; Cl, 6·9%).

The following were obtained similarly : ω-p-*chlorophenyl*-ω-(4-*chloro*-5-p-*chlorophenylazo*-2-*dimethylamino*-6-*pyrimidylamino*)*acetophenone*, m. p. 248° (decomp.) (from butanol) (Found : C, 58·0; H, 3·7; Cl, 19·8. $C_{26}H_{21}ON_6Cl_3$ requires C, 57·8; Cl, 3·9; H, 19·8%), and ω-p-*chlorophenyl*-ω-(5-p-*chlorophenylazo*-2-*dimethylamino*-6-*pyrimidylamino*)*acetophenone*, m. p. 196° (from butanol) (Found : C, 60·5; H, 5·1; N, 19·0. $C_{27}H_{25}ON_7Cl_2$ requires C, 60·7; H, 4·7; N, 18·4%).

4-*Chloro*-ω-(5-p-*chlorophenylazo*-2-*dimethylamino*-4-*hydroxy*-6-*pyrimidylamino*)-ω-*phenylacetophenone*.—4-Chloro-ω-phenylacetophenone hydrochloride (14·1 g.) was dissolved in water (800 c.c.) and basified with ammonia. The free amino-ketone was collected, dried over phosphoric oxide, and added to a solution of 4-chloro-5-*p*-chlorophenylazo-2-dimethylamino-4-hydroxypyrimidine (7·8 g.) in dimethylformamide (400 c.c.). After 24 hours' stirring at room temperature the separated solid was collected and crystallised from dimethylformamide–ethanol. The *ketone* (7 g.) had m. p. 239° (Found : C, 60·0; H, 4·8; N, 16·4; Cl, 13·5. $C_{26}H_{22}O_2N_6Cl_2$ requires C, 59·9; H, 4·2; N, 16·1; Cl, 13·6%).

Ethyl 4-*Amino*-5-p-*chlorophenylazo*-2-*dimethylamino*-6-*pyrimidylaminoacetate*.—To a solution of glycine ethyl ester (5·6 g.) in ethanol (100 c.c.), 4-amino-6-chloro-5-*p*-chlorophenylazo-2-dimethylaminopyrimidine (5·5 g.) in dioxan (150 c.c.) was added and the whole heated under reflux for 8 hr. Unchanged pyrimidine which separated on cooling was filtered off and the filtrate diluted with water. The precipitated solid was collected, crystallised from ethyl acetate–light petroleum (b. p. 60—80°), and recrystallised from ethanol, to give the *ester* (2 g.), m. p. 139° (Found : C, 50·9; H, 5·0; N, 26·1. $C_{16}H_{20}O_2N_7Cl$ requires C, 50·9; H, 5·3; N, 26·0%). Further examples of compounds of this type are given in B.P. 763,043. *Ethyl* 5-p-*chlorophenylazo*-2-*dimethylamino*-4-*hydroxy*-6-*pyrimidylaminoacetate*, m. p. 218° (Found : C, 50·7; H, 5·2; N, 22·6; Cl, 9·6. $C_{16}H_{19}O_3N_6Cl$ requires C, 50·7; H, 5·0; N, 22·1; Cl, 9·4%), was prepared similarly.

Ethyl 4-*Chloro*-5-p-*chlorophenylazo*-2-*methylamino*-6-*pyrimidylaminoacetate*.—*p*-Chlorobenzenediazonium chloride (17 c.c. of 0·01M-solution) was added to a solution of ethyl 4-chloro-2-methylamino-6-pyrimidylaminoacetate (2·5 g.) in 50% acetic acid (160 c.c.) containing crystalline sodium acetate (10 g.). After 12 hours' stirring the *azo-compound* was collected and crystallised from butanol; it (2 g.) had m. p. 218° (Found : C, 46·7; H, 4·4; N, 22·6.

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$C_{15}H_{16}O_2N_6Cl_2$ requires C, 47·0; H, 4·2; N, 21·9%). *Ethyl* 4-*chloro*-5-p-*chlorophenylazo*-2-*dimethylamino*-6-*pyrimidylaminoacetate*, m. p. 214° (from dioxan) (Found : C, 48·4; H, 4·5; N, 20·7; Cl, 18·4. $C_{16}H_{18}O_2N_6Cl_2$ requires C, 48·3; H, 4·6; N, 21·1; Cl, 17·9%), was obtained similarly.

7 : 8-*Dihydropteridines*.—2-*Dimethylamino*-7 : 8-*dihydro*-4-*hydroxy*-6-*phenylpteridine*. ω-(5-*p*-Chlorophenylazo-2-dimethylamino-4-hydroxy-6-pyrimidylamino)acetophenone (1·2 g.) in glacial acetic acid (60 c.c.) was treated at the b. p. in an atmosphere of nitrogen with zinc dust (1·1 g.). The mixture was heated for a further 1 hr., then filtered hot. Removal of the solvent under reduced pressure gave an oil which was triturated with ether and filtered. The residue after being washed with ether was dissolved in dilute hydrochloric acid, and the solution evaporated under reduced pressure. The hydrochloride was triturated with ethyl acetate, collected, and dissolved in water. Basification of this solution with ammonia gave the base (0·1 g.) which after crystallisation from ethanol as the *hemihydrate* had m. p. 311° (Found : C, 60·1; H, 5·9; N, 25·0. $C_{14}H_{15}ON_5,\frac{1}{2}H_2O$ requires C, 60·4; H, 5·8; N, 25·2%), $\lambda_{max.}$ 270 mμ ($E^{1\%}_{1\,cm.}$ 750 in N-HCl). The following were made similarly : 2 : 4-*bisdimethylamino*-7 : 8-*dihydro*-6 : 7-*diphenylpteridine*, m. p. 278° (Found : N, 20·0; Cl, 8·8. $C_{22}H_{23}N_6Cl$ requires N, 20·6; Cl, 8·7%); 7-*p*-chlorophenyl-2-dimethylamino-7 : 8-dihydro-4-methylamino-6-phenylpteridine, m. p. 267—269° (although not obtained analytically pure it was oxidised satisfactorily to the pteridine, see below); 6-p-*chlorophenyl*-2-*dimethylamino*-7 : 8-*dihydro*-4-*hydroxy*-7-*phenylpteridine hydrochloride*, m. p. 346° (Found : C, 57·4; H, 5·0. $C_{20}H_{19}ON_5Cl,HCl$ requires C, 57·7; H, 4·6%).

6-p-*Chlorophenyl*-2-*dimethylamino*-7 : 8-*dihydro*-4-*hydroxypteridine*. 4-Chloro-ω-(5-*p*-chlorophenylazo-2-dimethylamino-4-hydroxy-6-pyrimidylamino)acetophenone (2·95 g.) in dimethylformamide (300 c.c.) was shaken in hydrogen (initial presssure 2 atm.) for 2 hr. in presence of Raney nickel (5 g.). After removal of the catalyst and solvent the residue was triturated with ether and the solid collected. Crystallisation and recrystallisation from aqueous dimethylformamide gave the *pteridine* (1·8 g.), m. p. 370° (Found : C, 55·0; H, 4·3; N, 22·5; Cl, 11·8. $C_{14}H_{14}ON_5Cl$ requires C, 55·4; H, 4·6; N, 23·1; Cl, 11·8%).

In the following case the dihydro-compound was oxidised during manipulation :

2-*Dimethylamino*-4-*hydroxy*-7-*phenylpteridine*. α-(5-*p*-Chlorophenylazo-2-dimethylamino-4-hydroxy-6-pyrimidylamino)-α-phenylacetaldehyde dimethyl acetal (5 g.) was treated in glacial acetic acid (100 c.c.) with concentrated hydrochloric acid (10 c.c.). After 1 hr. at room temperature water was added and the precipitate collected. The crude aldehyde was reduced directly with hydrogen in the presence of Raney nickel as above. After removal of the catalyst and solvent the oily residue was mixed with glacial acetic acid (10 c.c.) and triturated twice with ether. The oil remaining was dissolved in 2N-hydrochloric acid ; the white solid which separated after a short while was suspended in water and treated with dilute ammonia until the mixture was just alkaline to Brilliant Yellow. The *pteridine* (2·3 g.) was collected and crystallised from aqueous dimethylformamide, having m. p. 326° (decomp.) (Found : C, 62·9; H, 4·9; N, 25·8. $C_{14}H_{13}ON_5$ requires C, 62·9; H, 4·9; N, 26·2%). $\lambda_{max.}$ 355 mμ ($E^{1\%}_{1\,cm.}$ 800 in N-HCl).

4-*Amino*-2-*dimethylamino*-6-*hydroxy*-5-*phenacylideneaminopyrimidine*.—4 : 5-Diamino-2-dimethylamino-6-hydroxypyrimidine sulphate (10·7 g.), phenylglyoxal monohydrate (6·1 g.), crystalline sodium acetate (27 g.), and 50% (v/v) ethanol (400 c.c.) were heated under reflux for 15 min. The solid which separated on cooling was collected and crystallised from ethanol, to give the *aldimine* (7·5 g.), m. p. 267° (decomp.) (Found : C, 59·1; H, 5·5; N, 24·2. $C_{14}H_{15}O_2N_5$ requires C, 59·0; H, 5·3; N, 24·5%).

2-*Amino*-3-N-*methylcarbamoyl*-5 : 6-*diphenylpyrazine*.—Methyl 3-amino-5 : 6-diphenylpyrazine-2-carboxylate (1 g.) was heated for 16 hr. at 160° with methylamine (10 g.) in ethanol (55 c.c.). After removal of the solvent the residue was crystallised from ethanol, to give the *amide* (0·5 g.), m. p. 197—198° (Found : C, 71·0; H, 5·4; N, 18·5. $C_{16}H_{16}ON_4$ requires C, 71·1; H, 5·3; N, 18·4%).

2 : 4-*Disubstituted Pteridines*.—These have been made by a number of methods of which the examples given are typical; details of other compounds are given in Table 4; additional examples are recorded in B.P. 763,044.

(1) *Oxidation of a* 7 : 8-*dihydropteridine*. 2-*Dimethylamino*-4-*hydroxy*-6-*phenylpteridine*. To 2-dimethylamino-7 : 8-dihydro-4-hydroxy-6-phenylpteridine (0·2 g.) in 0·5N-sodium hydroxide (50 c.c.), potassium permanganate (0·1 g.) in water (15 c.c.) was added with stirring during 15 min. After a further 1·5 hr., ethanol was added to destroy excess of permanganate, and the manganese dioxide was removed by filtration and washed. The filtrate and washings were

TABLE 1. 2 : 6-*Diamino*-5-*arylazo*-4-*chloropyrimidines* (as III ; Z = Cl).

Required (%) Found (%)

TABLE 1. 2 : 6-*Diamino*-5-*arylazo*-4-*chloropyrimidines* (as III; Z = Cl).

X	Y	Ar	M. p.	Solvent *	Yield (%)	Found (%) C	H	N	Cl	Formula	Required (%) C	H	N	Cl
NH_2	NHMe	*p*-C_6H_4Cl	255°	DMF	47	44·4	3·3	28·0	—	$C_{11}H_{10}N_6Cl_2$	44·4	3·4	28·3	—
NH_2	NMe_2	,,	204	DMF–EtOH	65	46·3	3·8	27·4	—	$C_{12}H_{12}N_6Cl_2$	46·3	3·9	27·0	—
NHMe	NH_2	,,	272 d	DMF	90	44·4	3·5	—	24·1	$C_{11}H_{10}N_6Cl_2$	44·4	3·4	—	23·9
NHMe	NHMe	,,	272	DMF–MeOH	95	46·4	3·8	27·4	22·9	$C_{12}H_{12}N_6Cl_2$	46·3	3·9	27·0	22·8
NHEt	NHMe	,,	214	BuOH	75	48·0	3·8	25·9	21·1	$C_{13}H_{14}N_6Cl_2$	48·0	4·3	25·8	21·9
NMe_2	NH_2	,,	229	BuOH	90	45·9	3·7	27·2	22·6	$C_{12}H_{12}N_6Cl_2$	46·3	3·9	27·0	22·8
NMe_2	NHMe	Ph	163	EtOH	78	53·7	5·2	28·9	—	$C_{18}H_{18}N_6Cl$	54·0	5·1	28·2	—
NMe_2	NHMe	*p*-C_6H_4Cl	183	BuOH	90	47·8	4·2	26·0	21·7	$C_{13}H_{14}N_6Cl_2$	48·0	4·3	25·8	21·8
$Me_2N{\cdot}[CH_2]_3{\cdot}NH$	NHMe	,,	158	EtOH	50	49·6	5·3	26·1	19·0	$C_{15}H_{18}N_7Cl_2$	49·1	4·9	26·7	19·3

* DMF = dimethylformamide.

TABLE 2. 2 : 4 : 6-*Triamino*-5-p-*chlorophenylazopyrimidines* (III; Z = NH_2).

X	Y	M. p.	Solvent *	Starting material: I; Y =	Yield (%)	Found (%) C	H	N	Cl	Formula	Required (%) C	H	N	Cl
NH_2	NHMe	213°	BuOH	NH_2, NHMe	40, 80	47·9	4·1	34·4	—	$C_{11}H_{12}N_7Cl$	47·6	4·3	35·3	—
NH_2	NMe_2	205	DMF–H_2O	NH_2	96	49·9	5·0	33·5	11·7	$C_{12}H_{14}N_7Cl$	49·5	4·8	33·6	12·2
NH_2	$Et_2N{\cdot}[CH_2]_3{\cdot}NH$	139	EtOH–H_2O	NH_2	44	54·8	6·9	29·4	9·0	$C_{17}H_{26}N_8Cl$	54·5	7·0	29·9	9·5
NHMe	NH_2	241	BuOH	NH_2	70	47·7	4·6	35·2	—	$C_{11}H_{12}N_7Cl$	47·6	4·3	35·3	—
NHMe	NHMe	197	EtAc	NH_2, NHMe	85, 92	49·8	4·8	33·6	12·5	$C_{12}H_{14}N_7Cl$	49·5	4·8	33·6	12·2
NHMe	NMe_2	184	DMF–H_2O	NH_2 †	90, 79 †	51·6	5·5	32·0	—	$C_{13}H_{16}N_7Cl$	51·1	5·2	32·1	—
NHEt	NHMe	161	BuOH	NHMe	80	51·1	5·2	31·7	11·9	$C_{13}H_{16}N_7Cl$	51·1	5·2	32·1	11·6
NMe_2	NHMe	193	BuOH	NMHe	90	51·6	5·1	32·3	11·8	$C_{13}H_{16}N_7Cl$	51·1	5·2	32·1	11·6
NMe_2	NMe_2	203	BuOH	NH_2, NMe_2	95, 93	52·7	6·0	30·1	11·3	$C_{14}H_{18}N_7Cl$	52·6	5·6	30·7	11·1
NMe_2	$[CH_2]_5{>}N$	175	BuOH	NH_2	86	56·7	5·5	27·7	10·4	$C_{17}H_{23}N_7Cl$	56·7	6·1	27·3	9·9
NMe_2	$O{<}[CH_2]_4{>}N$	183	BuOH	NH_2	91	52·9	5·5	27·4	9·8	$C_{16}H_{20}ON_7Cl$	53·1	5·5	27·1	9·8
NMe_2	$Et_2N{\cdot}[CH_2]_2{\cdot}NH$	150	60—80° Pet	NH_2	44	55·5	6·7	28·8	9·1	$C_{16}H_{27}N_8Cl$	55·3	6·9	28·7	9·1
$Me_2N{\cdot}[CH_2]_3{\cdot}NH$	NHMe	144	100—120° Pet	NHMe	90	52·4	6·3	31·9	10·3	$C_{15}H_{21}N_8Cl$	51·7	6·0	32·1	10·2

* DMF = dimethylformamide; Pet = light petroleum of stated b. p. † Prepared by direct reaction of (I; Y = NH_2) with alcoholic dimethylamine and also from (I; Y = NH_2) and ammonia in dimethylformamide.

TABLE 3. *Tetra-aminopyrimidines* (II; Z = NH_2).

X	Y	M. p.*	Solvent	Yield (%)	Found (%) C	H	N	S	Formula	Required (%) C	H	N	S
NH_2	NHMe	250°d	H_2O	89	27·2	6·0	37·3	7·2	$C_5H_{10}N_6{\cdot}\frac{1}{2}H_2OSO_4{\cdot}H_2O$	27·2	5·9	38·0	7·2
NH_2	NMe_2	209	H_2O–EtOH	48	26·3	5·5	—	11·1	$C_6H_{12}N_6{\cdot}H_2SO_4{\cdot}\frac{1}{2}H_2O$	26·2	5·5	—	11·6
NHMe	NH_2	255d	H_2O	75	23·7	4·8	31·8	12·3	$C_5H_{10}N_6{\cdot}H_2SO_4$	23·8	4·8	33·3	12·7
NHMe	NHMe	259	H_2O–EtOH	80	26·3	5·9	30·4	11·0	$C_6H_{12}N_6{\cdot}H_2SO_4{\cdot}\frac{1}{2}H_2O$	26·2	5·5	30·5	11·6
NHMe	NMe_2	193	H_2O–EtOH	65	29·1	5·8	28·6	10·5	$C_7H_{14}N_6{\cdot}H_2SO_4{\cdot}\frac{1}{2}H_2O$	29·1	5·9	29·1	11·1
NHEt	NHMe	293d	H_2O–EtOH	49	28·4	6·1	28·4	—	$C_7H_{14}N_6{\cdot}H_2SO_4{\cdot}H_2O$	28·2	6·0	28·2	—
NMe_2	NH_2	314d	H_2O	58	27·3	5·4	31·2	11·9	$C_6H_{12}N_6{\cdot}H_2SO_4$	27·1	5·3	31·6	12·1
NMe_2	NHMe	273d	H_2O	64	29·7	5·8	30·5	11·6	$C_7H_{14}N_6{\cdot}H_2SO_4$	30·0	5·7	30·0	11·4
NMe_2	NMe_2	182d	EtOH	38	29·6	6·3	27·0	9·6	$C_8H_{16}N_6{\cdot}H_2SO_4{\cdot}\frac{1}{2}H_2O$	29·9	6·5	26·2	10·0
NMe_2	$[CH_2]_5{>}N$	208d	H_2O–EtOH	33	35·0	6·2	22·2	12·0	$C_{11}H_{20}N_6{\cdot}1{\cdot}5H_2SO_4$	34·5	6·0	21·9	12·5
NMe_2	$O{<}[CH_2]_4{>}N$	194d	H_2O–EtOH	57	35·7	5·7	—	9·3	$C_{10}H_{18}ON_6{\cdot}H_2SO_4$	35·7	6·0	—	9·5

* d = with decomp.

TABLE 4. 2 : 4-*Disubstituted pteridines* (I).

X	Y	R	R′	M. p.*	Solvent †	Prep.	Yield (%)	Found (%) C	H	N	Cl	Formula	Required (%) C	H	N	Cl
NH_2	NHMe	H	H	248°	H_2O	2*c*	26	47·8	4·2	47·5	—	$C_7H_8N_6$	47·7	4·5	47·7	—
NH_2	NHMe	Ph	Ph	272	EtOH	2*c*, 3	73, 5	69·4	4·9	24·8	—	$C_{19}H_{16}N_6$	69·5	4·9	25·6	—
NH_2	NMe_2	Ph	Ph	322 d	DMF	2*c*	63	69·4	5·5	24·3	—	$C_{20}H_{18}N_6$	70·1	5·5	24·6	—
NH_2	$Et_2N{\cdot}[CH_2]_2{\cdot}NH$	Ph	Ph	201 ‡	EtOH	2*c*	50	70·1	6·5	23·6	—	$C_{25}H_{30}N_7$	70·3	6·8	23·0	—
NHMe	OH	Ph	H	356 d [1]	DMF	2*b*	75	61·0	4·6	28·0	—	$C_{13}H_{11}ON_5$	61·7	4·4	27·7	—
NHMe	OH	H	Ph	387 d	DMF	2*a*, 4	80, 52	61·7	4·4	27·3	—	$C_{13}H_{11}ON_5$	61·7	4·4	27·7	—
NHMe	OH	*p*-C_6H_4Cl	H	370 d	DMF–EtOH	1, 2*b*	50, 26	54·7	3·6	23·6	13·2	$C_{13}H_{10}ON_5Cl$	54·3	3·5	24·1	12·4
NHMe	OH	H	*p*-C_6H_4Cl	363 d	DMF	2*a*, 4	65, 80	53·9	3·8	23·2	11·7	$C_{13}H_{10}ON_5Cl$	54·3	3·5	24·1	12·4
NHMe	OH	Ph	Ph	365 d	DMF	4	80	69·4	4·7	22·0	—	$C_{19}H_{15}ON_5$	69·3	4·6	22·0	—
NHMe	NH_2	H	H	242	H_2O	2*c*	72	47·4	4·4	47·7	—	$C_7H_8N_6$	47·7	4·5	47·7	—
NHMe	NH_2	Me	Me	281	EtOH	2*c*	51	53·1	6·1	41·3	—	$C_9H_{12}N_6$	52·9	5·9	41·2	—
NHMe	NH_2	Ph	Ph	307	DMF	2*c*	75	69·3	5·5	25·8	—	$C_{19}H_{16}N_6$	69·5	4·9	25·6	—
NHMe	NHMe	H	H	214	EtOH	2*c*	50	50·8	5·6	44·0	—	$C_8H_{10}N_6$	50·5	5·3	44·2	—
NHMe	NHMe	Me	Me	266	EtOH	2*c*	28	54·9	6·9	38·2	—	$C_{10}H_{14}N_6$	55·1	6·4	38·5	—
NHMe	NHMe	Ph	H	264	DMF	3	32	63·3	5·4	31·4	—	$C_{14}H_{14}N_6$	63·2	5·2	31·6	—
NHMe	NHMe	H	Ph	256 [2]	MeOH	2*b*	30	63·3	5·5	31·2	—	$C_{14}H_{14}N_6$	63·2	5·2	31·6	—
NHMe	NHMe	H	*p*-C_6H_4Cl	294 [2]	DMF	2*b*	25	55·6	4·4	27·9	11·5	$C_{14}H_{13}N_6Cl$	55·9	4·3	28·0	11·8
NHMe	NHMe	Ph	Ph	262	DMF–EtOH	2*c*	49	70·3	5·3	24·6	—	$C_{20}H_{18}N_6$	70·1	5·3	24·6	—
NHMe	NHMe	*o*-C_6H_4Cl	*o*-C_6H_4Cl	265	BuOH	2*c*	22	58·8	3·2	—	—	$C_{20}H_{16}N_6Cl_2$	58·4	3·9	20·4	17·3
NHMe	NHMe	*m*-C_6H_4Cl	*m*-C_6H_4Cl	256	MeOH	2*c*	31	58·3	3·8	20·1	17·1	$C_{20}H_{16}N_6Cl_2$				
NHMe	NHMe	*p*-C_6H_4Cl	*p*-C_6H_4Cl	323	DMF	2*c*	63	58·5	4·0	20·6	17·2	$C_{20}H_{16}N_6Cl_2$				
NHMe	NHMe	*p*-MeO·C_6H_4	*p*-MeO·C_6H_4	259	EtOH	2*c*	24	65·1	5·4	20·9	—	$C_{22}H_{22}O_2N_6$	65·7	5·5	20·9	—
NHMe	NHMe	3 : 4-CH_2O_2:C_6H_3	3 : 4-CH_2O_2:C_6H_3	297	EtOH–DMF	2*c*	28	60·9	4·3	19·5	—	$C_{22}H_{18}O_4N_6$	61·4	4·2	19·5	—
NHMe	NHMe	9 : 10-Phenanthrylene		311	DMF	2*c*	66	70·5	4·7	24·4	—	$C_{20}H_{16}N_6$	70·6	4·7	24·7	—
NHMe	NHMe	7 : 8-Acenaphthylene		307	DMF	2*c*	40	65·9	5·0	25·9	—	$C_{18}H_{14}N_6,H_2O$	65·1	4·8	25·3	—
NHMe	NHMe	2-Furyl	2-Furyl	218	EtOAc	2*c*	24	59·6	4·2	25·7	—	$C_{16}H_{14}O_2N_6$	59·6	4·4	26·1	—
NHMe	NHMe	2 : 3-Indolo		338	DMF	2*c*	75	58·7	5·0	33·9	—	$C_{14}H_{13}N_7,\frac{1}{2}H_2O$	58·3	4·9	34·0	—
NHMe	NMe_2	Ph	Ph	306	DMF	2*c*	60	70·4	5·6	24·1	—	$C_{21}H_{20}N_6$	70·8	5·6	23·6	—
NHEt	NHMe	Ph	Ph	249	EtOH	2*c*	21	70·7	6·1	23·3	—	$C_{21}H_{20}N_6$	70·8	5·6	23·6	—
NMe_2	OH	Ph	H	336 d	EtOH	1, 2*a*, 4	15, 90	62·5	4·8	26·6	—	$C_{14}H_{13}ON_5$	62·9	4·4	26·4	—
NMe_2	OH	H	Ph	325 d	DMF–EtOH	1, 2*b*, 4	65, 90, 90	63·0	4·8	26·0	—	$C_{14}H_{13}ON_5$	62·9	4·4	26·4	—
NMe_2	OH	*p*-C_6H_4Cl	H	377 d	DMF–EtOH	1	85	55·8	4·0	23·9	11·7	$C_{14}H_{12}ON_5Cl$	55·7	4·0	23·2	11·8
NMe_2	OH	Ph	Ph	361	DMF–EtOH	2*c*	33	69·9	5·0	20·6	—	$C_{20}H_{17}ON_5$	70·0	5·0	20·4	—
NMe_2	OH	*p*-C_6H_4Cl	Ph	350	BuOH	1	85	63·9	4·3	18·6	9·4	$C_{20}H_{16}ON_5Cl$	63·5	4·2	18·5	9·4
NMe_2	OEt	Ph	H	200	MeOH	EtOH on 4-Cl-compound	30	65·3	6·1	23·7	—	$C_{16}H_{17}ON_5$	65·1	5·8	23·7	—
NMe_2	NH_2	Ph	Ph	239	BuOH	2*c*	63	69·9	5·1	25·0	—	$C_{20}H_{18}N_6$	70·2	5·3	24·6	—
NMe_2	NHMe	Ph	Ph	205	EtOAc	2*c*	43	69·1	5·9	23·7	—	$C_{21}H_{20}N_6$	70·8	5·6	23·6	—
NMe_2	NHMe	Ph	*p*-C_6H_4Cl	239	EtOH	1	70	64·0	4·9	21·5	9·2	$C_{21}H_{19}N_6Cl$	64·6	4·9	21·5	9·1
NMe_2	NMe_2	Pr^i	Pr^i	150	EtOH–H_2O	2*c*	30	63·7	8·1	28·2	—	$C_{16}H_{26}N_6$	63·6	8·6	27·8	—
NMe_2	NMe_2	Ph	H	188	EtOH	2*a*, 3	29, 40	65·7	6·4	28·1	—	$C_{16}H_{18}N_6$	65·3	6·1	28·6	—
NMe_2	NMe_2	H	Ph	191	EtOH	2*b*, 3	37, 80	65·4	6·4	28·5	—	$C_{16}H_{18}N_6$	65·3	6·1	28·6	—
NMe_2	NMe_2	Ph	Ph	211	EtOAc	2*c*	55	71·3	6·2	23·2	—	$C_{22}H_{22}N_6$	71·4	5·9	22·7	—
NMe_2	$[CH_2]_5{>}N$	Ph	Ph	207	EtOH–H_2O	2*c*	75	73·6	6·4	21·0	—	$C_{25}H_{26}N_6$	73·3	6·3	20·5	—
NMe_2	$O{<}[CH_2]_4{>}N$	Ph	Ph	216	EtOH	2*c*	71	69·5	6·0	20·4	—	$C_{24}H_{24}ON_6$	69·9	5·8	20·4	—

* d = with decomp. † DMF = dimethylformamide. ‡ Potter and Henshall record m. p. 195—196° for this substance prepared by a different route.

[1] $\lambda_{max.}$ 280 ($E^{1\%}_{1\,cm.}$ 966), 350 mμ ($E^{1\%}_{1\,cm.}$ 566). [2] $\lambda_{max.}$ 365 mμ ($E^{1\%}_{1\,cm.}$ 950). [3] $\lambda_{max.}$ 365 mμ ($E^{1\%}_{1\,cm.}$ 925).

concentrated to about 50 c.c., acidified to Congo-red with hydrochloric acid and then neutralised with ammonia. The *pteridine*, crystallised from ethanol, had m. p. 322° (decomp.) (Found: C, 62·5; H, 4·8; N, 25·5. $C_{14}H_{13}ON_5$ requires C, 62·9; H, 4·9; N, 26·2%), $\lambda_{max.}$ 280 ($E_{1\,cm.}^{1\%}$ 910), 355 mμ ($E_{1\,cm.}^{1\%}$ 395).

(2) *Condensation of a* 4 : 5-*diaminopyrimidine with an* α-*diketone.* (*a*) With phenylglyoxal at pH >4. 2-Dimethylamino-4-hydroxy-7-phenylpteridine, identical in m. p. and mixed m. p. with the product obtained by reduction, was obtained by warming 4-amino-2-dimethylamino-6-hydroxy-5-phenacylideneaminopyrimidine with dilute sodium hydroxide. Acidification of the mixture with acetic acid gave the pteridine.

The preparation of 2 : 4-bisdimethylamino-7-phenylpteridine is typical of those cases in which the intermediate compound is not isolated: 4 : 5-Diamino-2 : 6-bisdimethylaminopyrimidine sulphate (2·94 g.), crystalline sodium acetate (6·8 g.), phenylglyoxal monohydrate (1·5 g.), and 50% v/v ethanol were heated under reflux for 15 min. The solid which separated on cooling was collected, dissolved in 2N-acetic acid, and the solution filtered (charcoal). The *pteridine* was precipitated from the filtrate with ammonia and, crystallised from butanol and then from ethanol, had m. p. 191° (Found: C, 65·4; H, 6·4; N, 28·5. $C_{16}H_{18}N_6$ requires C, 65·3; H, 6·1; N, 28·6%).

(*b*) With phenylglyoxal at pH < 1. 2-Dimethylamino-4-hydroxy-6-phenylpteridine. 4 : 5-Diamino-2-dimethylamino-6-hydroxypyrimidine sulphate (7·43 g.), 6N-sulphuric acid (250 c.c.), phenylglyoxal monohydrate (3·7 g.), and ethanol (250 c.c.) were heated under reflux for 2 hr. After removal of the ethanol under reduced pressure the solution was cooled in ice, basified with ammonia, and separated from a small flocculent precipitate. The *pteridine* which separated on acidification to litmus with dilute acetic acid was collected and crystallised from dimethylformamide–ethanol. It had m. p. 332° (Found: C, 62·5; H, 4·8; N, 27·0. $C_{14}H_{13}ON_5$ requires C, 62·9; H, 4·4; N, 26·4%).

(*c*) With a symmetrically substituted α-diketone. 4-Methylamino-2 : 5 : 6-triaminopyrimidine sulphate (10·8 g.), benzil (14·8 g.), crystalline sodium acetate (24 g.), ethanol (400 c.c.), and water (100 c.c.) were heated under reflux for 5 hr. The product which separated on cooling was collected and extracted with 0·5N-hydrochloric acid. Basification of the extract with ammonia gave 2-*amino*-4-*methylamino*-6 : 7-*diphenylpteridine* which, crystallised from ethanol, had m. p. 272° (Found: C, 69·4; H, 4·9; N, 25·8. $C_{19}H_{16}N_6$ requires C, 69·5; H, 4·9; N, 25·6%).

(3) *Replacement of a* 4-*hydroxy- by a* 4-*amino*(*or substituted amino*)-*group* via *the chloro-compound.* 2-Amino-4-methylamino-6 : 7-diphenylpteridine, identical (m. p. and mixed m. p.) with the above, was obtained as follows: 2-Amino-4-hydroxy-6 : 7-diphenylpteridine (2 g.) and redistilled phosphorus oxychloride (120 c.c.) were heated under reflux for 2 hr. After removal of excess of phosphorus oxychloride under reduced pressure, the residual glass was heated with 2·5M-ethanolic methylamine (100 c.c.) for 1 hr. The dark red oily solid which remained after removal of the solvent was extracted with 0·5N-hydrochloric acid. The pteridine was isolated from this extract as above.

In a similar sequence of reactions with 2-dimethylamino-4-hydroxy-6-phenylpteridine and alcoholic dimethylamine, in addition to 2 : 4-*bisdimethylamino*-6-*phenylpteridine* (m. p. 190°; from methanol) (Found: C, 65·7; H, 6·4; N, 28·1. $C_{16}H_{18}N_6$ requires C, 65·3; H, 6·1; N, 28·6%), which was extracted from the crude dimethylamination product with 2N-acetic acid, there was also obtained 2-*dimethylamino*-4-*ethoxy*-6-*phenylpteridine*, m. p. 200° (from ethanol) (Found: C, 65·3; H, 6·1; N, 23·7. $C_{16}H_{17}ON_5$ requires C, 65·1; H, 5·8; N, 23·7%). By using the conditions of Cain *et al.*[9] there was obtained from 2-amino-4-hydroxy-6 : 7-diphenyl pteridine a product, m. p. 253—259°. Extraction of this with 1·5N-acetic acid left 2-amino-3-*N*-methylcarbamoyl-5 : 6-diphenylpyrazine, m. p. and mixed m. p. 197—198° with an authentic sample (after crystallisation from ethanol). Basification of the extract with ammonia and crystallisation of the precipitate from ethanol gave 2 : 4-*bismethylamino*-6 : 7-*diphenylpteridine*, m. p. 266—267°, undepressed on admixture with an authentic sample obtained by condensation of 4 : 5-diamino-2 : 6-bismethylaminopyrimidine with benzil (Found: C, 70·3; H, 5·3; N, 24·6. $C_{20}H_{18}N_6$ requires C, 70·1; H, 5·3; N, 24·6%). The same product was obtained by reaction between 4-amino-2-mercapto-6 : 7-diphenylpteridine and alcoholic methylamine under the conditions described by Taylor and Cain.[10] Repetition of the similar reaction between 4-amino-2-mercapto-6 : 7-diphenylpteridine and alcoholic dimethylamine gave a product, m. p. 186—215° (Taylor and Cain give m. p. 192—195°): trituration of this with cold 0·5N-acetic acid left a residue which on repeated crystallisation from methanol had m. p. 211° undepressed

* d = with decomp. † DMF = dimethylformamide. ‡ Potter and Henshall record m. p. 195—196° for this substance prepared by a different route.
[1] $\lambda_{max.}$ 280 ($E_{1\,cm.}^{1\%}$ 966), 350 mμ ($E_{1\,cm.}^{1\%}$ 566). [2] $\lambda_{max.}$ 365 mμ ($E_{1\,cm.}^{1\%}$ 950). [3] $\lambda_{max.}$ 365 mμ ($E_{1\,cm.}^{1\%}$ 925).

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on admixture with an authentic sample of 2 : 4-*bisdimethylamino*-6 : 7-*diphenylpteridine* (Found : C, 71·3; H, 6·2; N, 23·2. $C_{22}H_{22}N_6$ requires C, 71·4; H, 5·9; N, 22·7%) obtained by condensation of 4 : 5-diamino-2 : 6-bisdimethylaminopyrimidine and benzil. Basification of the acetic acid extract with ammonia gave a substance, m. p. 221—228° raised to 236° by crystallisation from butanol and undepressed on admixture with an authentic sample of 4-*amino*-2-*dimethylamino*-6 : 7-*diphenylpteridine* (Found : C, 69·9; H, 5·1; N, 25·0. $C_{20}H_{18}N_6$ requires C, 70·2; H, 5·3; N, 24·6%), obtained by condensation of 4 : 5 : 6-triamino-2-dimethylaminopyrimidine and benzil.

(4) *Hydrolysis of a* 4-*amino*(*or substituted amino*)*pteridine.* 2 : 4-Bismethylamino-7-phenylpteridine (0·3 g.) and 6N-hydrochloric acid (50 c.c.) were heated under reflux for 20 hr. After cooling to about 50°, the solution was made faintly alkaline to Brilliant Yellow by ammonia. 4-*Hydroxy*-2-*methylamino*-7-*phenylpteridine* was collected, washed with water, dried, and crystallised from dimethylformamide; it had m. p. 387° (decomp.) undepressed on admixture with a sample prepared by method 2*a* (Found : C, 61·7; H, 4·4; N, 27·3. $C_{13}H_{11}ON_5$ requires C, 61·7; H, 4·4; N, 27·6%); $\lambda_{max.}$ 250 mμ ($E^{1\%}_{1\ cm.}$ 700).

α-*Bromo*-α-*phenylacetaldehyde Dimethyl Acetal.**—To a solution of styryl acetate [12] in carbon tetrachloride (290 c.c.), bromine (39 c.c.) in carbon tetrachloride (40 c.c.) was added with stirring below 10° during 1½ hr. Methanol (290 c.c.) was then added and stirring continued for a further 12 hr. at this temperature. After a further 48 hr. the mixture was poured into ice-water. The oil which separated was collected, washed with 5% w/w sodium hydrogen carbonate solution, dried ($MgSO_4$), and distilled in presence of a little anhydrous sodium carbonate. The *acetal* (122 g.) had b. p. 138—140°/14 mm.

α-*Benzylamino*-α-*phenylacetaldehyde Dimethyl Acetal.**—α-Bromo-α-phenylacetaldehyde dimethyl acetal (122 g.), benzylamine (183 g.), and a trace of sodium iodide were heated to 140° during 1 hr. When the reaction had moderated heating was continued at 160° for a further 2 hr. After cooling, the mixture was poured into water, and the product collected with ether, dried ($MgSO_4$), and distilled. The *base* (89 g.) had b. p. 121—148°/0·2 mm. (Found : N, 5·7. $C_{17}H_{21}O_2N$ requires N, 5·2%).

α-*Amino*-α-*phenylacetaldehyde Dimethyl Acetal.**—The above benzylamino-compound was hydrogenated in methanol (300 c.c.) over 5% palladised charcoal (25 g.) at 100—105° with an initial hydrogen pressure of 95 atm. After removal of the catalyst the *aminoacetal* (47 g.), b. p. 134—136°/18 mm., was isolated by distillation (Found : C, 65·6; H, 8·2; N, 7·8. $C_{10}H_{15}O_2N$ requires C, 66·3; H, 8·3; N, 7·7%).

ω-*Aminoacetophenone Semicarbazone.**—ω-Aminoacetophenone hydrochloride (56 g.) was dissolved in ethanol (350 c.c.) with gentle warming and the solution cooled rapidly to room temperature. Semicarbazide (25 g.) was added and the mixture set aside for several hours. The prismatic crystals were filtered off and, crystallised from ethanol, had m. p. 107—108°.

α-*Amino*-4-*chlorodeoxybenzoin.*—To 4-chlorobenzyl phenyl ketone (28 g.) in dry ether (500 c.c.) saturated with hydrogen chloride at 0° butyl nitrite (7·5 g.) in ether (50 c.c.) was added. The hydroxyimino-compound which separated immediately was collected and crystallised from aqueous methanol. It had m. p. 121—123° and was reduced at room temperature and pressure in ethanol (350 c.c.) containing concentrated hydrochloric acid (12 c.c.) in presence of palladised charcoal. After removal of the catalyst and solvent the *amino-ketone hydrochloride* (6 g.) was crystallised from 2N-hydrochloric acid and then from methanol–ether; it had m. p. 248° (decomp.) (Found : C, 59·8; H, 4·5; N, 5·1; Cl, 26·0. $C_{14}H_{13}ONCl_2$ requires C, 59·6; H, 4·6; N, 5·0; Cl, 25·2%).

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* These experiments were carried out by Dr. W. G. M. Jones.

[12] Semmler, *Ber.*, 1909, **42**, 584.

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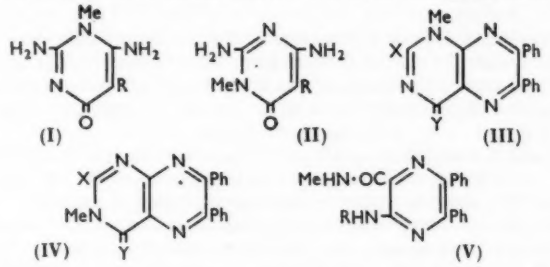
412. *Pteridines. Part V.* Derivatives of 1 : 4-Dihydro-1- and 3 : 4-Dihydro-3-methyl-6 : 7-diphenylpteridine.*

By W. R. Boon and G. Bratt.

The preparation of a number of derivatives of 1 : 4-dihydro-1- and 3 : 4-dihydro-3-methyl-6 : 7-diphenylpteridine is described. Condensation of methylguanidine with ethyl cyanoacetate gives 4-amino-6-hydroxy-2-methylaminopyrimidine and 2 : 6-diamino-1 : 4-dihydro-1-methyl-4-oxopyrimidine and not 2 : 6-diamino-3 : 4-dihydro-3-methyl-4-oxopyrimidine.

On condensation of methylguanidine with ethyl cyanoacetate, Roth, Smith, and Hultquist [1] obtained, in addition to 4-amino-6-hydroxy-2-methylaminopyrimidine, an isomeric substance to which they assigned the structure (II; R = H). This assignment was based on a comparison of the melting points of their two products with those obtained in a similar condensation of methylguanidine with ethyl acetoacetate.[2] Nitrosation of the presumed (II; R = H) followed by reduction and condensation with diacetyl gave a pteridine derivative whose infrared spectrum they considered to be in accord with the structure (IV; X = NH_2, Y = O, Me replacing Ph). We have now prepared 2-amino-1 : 4-dihydro-1-methyl-4-oxo-6 : 7-diphenylpteridine (III; X = NH_2, Y = O) and 2-amino-3 : 4-dihydro-3-methyl-4-oxo-6 : 7-diphenylpteridine (IV; X = NH_2, Y = O) by unambiguous methods for comparison with the product obtained by condensation between benzil and the triaminopyrimidine of Roth *et al.*



(I) (II) (III) (IV) (V)

5 : 6-Diamino-1 : 4-dihydro-2-mercapto-1-methyl-4-oxopyrimidine [3] with benzil gave 1 : 4-dihydro-2-mercapto-1-methyl-4-oxo-6 : 7-diphenylpteridine (III; X = SH, Y = O) which on reaction with ammonia or methylamine in presence of mercuric oxide was converted into the bases (III; X = NH_2 and NHMe, Y = O). The former product was identical with that obtained by condensation of benzil with the triaminopyrimidine of Roth *et al.* which must therefore have the constitution (I; R = NH_2). Hydrolysis of the product (III; X = NH_2, Y = O) yielded 1 : 4-dihydro-2-hydroxy-1-methyl-4-oxo-6 : 7-diphenylpteridine (III; X = OH, Y = O), also obtained by oxidation of the thiol (III; X = SH, Y = O) with hydrogen peroxide and by alkaline hydrolysis of the thioamide (III; X = NH_2, Y = S).

Treatment of the amide (III; X = NH_2 or MeNH, Y = O) with phosphorus pentasulphide in pyridine gave the thioamide (III; X = NH_2 or NHMe, Y = S). This reaction product, with methylamine and ammonia, gave the imino-derivatives (III; X = NH_2, Y = MeN and NH respectively), the latter identical with the product whose hydriodide had previously been obtained in these laboratories by Richardson [4] from 2 : 4-diamino-6 : 7-diphenylpteridine and methyl iodide.

* Part IV, preceding paper.

[1] Roth, Smith, and Hultquist, *J. Amer. Chem. Soc.*, 1951, **73**, 2864.
[2] Majima, *Ber.*, 1908, **41**, 176.
[3] Traube and Winter, *Arch. Pharm.*, 1906, **244**, 16.
[4] Dora N. Richardson, personal communication.

1 : 4-Dihydro-2-mercapto-1-methyl-6 : 7-diphenyl-4-thionopteridine was readily obtained from the thiol (III; X = SH, Y = O) and phosphorus pentasulphide.

2-Amino-5 : 6-diphenylpyrazine-3-carboxylic acid [5] was converted *via* its methyl ester into the methylamide (V; R = H) which with ethyl chloroformate gave the urethane (V; R = CO_2Et). This was then cyclised to the pteridine (IV; X = OH, Y = O) with sodium ethoxide.

Experimental

1 : 4-*Dihydro*-2-*mercapto*-1-*methyl*-4-*oxo*-6 : 7-*diphenylpteridine*.—5 : 6-Diamino-1 : 4-dihydro-2-mercapto-1-methyl-4-oxopyrimidine sulphate (7 g.), benzil (6 g.), and crystalline sodium acetate (18 g.) were heated under reflux for 6 hr. in 75% aqueous ethanol. The product which separated on cooling was collected, extracted with hot light petroleum (b. p. 100—120°), and crystallised from butanol to give the *pteridine* (7·4 g.), m. p. 289° (Found: C, 66·0; H, 4·2; N, 15·6; S, 9·6. $C_{19}H_{14}ON_4S$ requires C, 65·9; H, 4·1; N, 16·2; S, 9·3%).

2-*Amino*-1 : 4-*dihydro*-1-*methyl*-4-*oxo*-6 : 7-*diphenylpteridine*.—(*a*) 2 : 5 : 6-Triamino-1 : 4-dihydro-1-methyl-4-oxopyrimidine sulphate (6·3 g.), benzil (5·8 g.), and crystalline sodium acetate (17 g.) were heated under reflux for 6 hr. in 25% v/v aqueous ethanol. The *pteridine* which separated on cooling was collected and crystallised from dimethylformamide, and had m. p. 333° (decomp.) (10 g.) (Found: C, 67·5; H, 4·8; N, 20·6. $C_{19}H_{15}ON_5,0{\cdot}5H_2O$ requires C, 67·5; H, 4·7; N, 20·7%).

(*b*) 1 : 4-Dihydro-1-methyl-2-mercapto-4-oxo-6 : 7-diphenylpteridine (0·4 g.), yellow mercuric oxide (0·5 g.), butanol (70 c.c.), and chloroform (10 c.c.) were heated under reflux for 6 hr. in a slow stream of ammonia. The mixture was then filtered hot and evaporated under reduced pressure and the residue crystallised from dimethylformamide and then from ethanol; it was identical (m. p. and mixed m. p.) with the above product.

1 : 4-*Dihydro*-1-*methyl*-2-*methylamino*-4-*oxo*-6 : 7-*diphenylpteridine*, m. p. 307° (from ethanol) (Found: C, 69·8; H, 4·9; N, 20·0. $C_{20}H_{17}ON_5$ requires C, 69·9; H, 5·0; N, 20·4%), was obtained similarly in 40% yield by using methylamine in place of ammonia.

1 : 4-*Dihydro*-2-*hydroxy*-1-*methyl*-4-*oxo*-6 : 7-*diphenylpteridine*.—(*a*) 2-Amino-1 : 4-dihydro-1-methyl-4-oxo-6 : 7-diphenylpteridine (0·5 g.) and 2N-sodium hydroxide (50 c.c.) were heated under reflux for 4 hr. After cooling and acidification with acetic acid, the *hydroxy-compound* was collected and crystallised from aqueous ethanol; it (0·16 g.) had m. p. 280° (Found: C, 68·9; H, 4·2; N, 17·1. $C_{19}H_{14}O_2N_4$ requires C, 69·1; H, 4·3; N, 17·0%).

(*b*) To 1 : 4-Dihydro-2-mercapto-1-methyl-4-oxo-6 : 7-diphenylpteridine (0·9 g.) in N-potassium hydroxide, hydrogen peroxide (10 c.c. of 100-vol.) was added dropwise with stirring at 100°. The final pale yellow solution was cooled and acidified with acetic acid, and the product (0·3 g.) collected. After crystallisation from ethanol it had the same m. p. and mixed m. p. as above.

(*c*) 2-Amino-1 : 4-dihydro-1-methyl-6 : 7-diphenyl-4-thionopteridine (3 g.) in 2N-sodium hydroxide (300 c.c.) was heated under reflux for 4 hr. The crude product obtained by acidification after cooling was fractionally crystallised from methanol, to give the 2-hydroxy-4-oxo-compound (0·5 g.). A second product, m. p. 191°, not further investigated, was obtained by chromatography on alumina of the residue obtained on evaporation of the methanol mother-liquors.

2-*Amino*-1 : 4-*dihydro*-1-*methyl*-6 : 7-*diphenyl*-4-*thionopteridine*.—2-Amino-1 : 4-dihydro-1-methyl-4-oxo-6 : 7-diphenylpteridine (15 g.), phosphorus pentasulphide (19·5 g.), and pyridine (300 c.c.) were heated under reflux for 2 hr. The dark brown solid remaining after removal of the solvent under reduced pressure was extracted with 2% aqueous sodium hydroxide and crystallised twice from dimethylformamide, to give the *thione* (7·4 g.), m. p. 295° (decomp.) (Found: C, 66·2; H, 4·4; N, 20·3; S, 9·3. $C_{19}H_{13}N_5S$ requires C, 66·2; H, 4·5; N, 20·4; S, 9·0%). 1 : 4-*Dihydro*-1-*methyl*-2-*methylamino*-6 : 7-*diphenyl*-4-*thionopteridine*, m. p. 300° (decomp.) (from dimethylformamide) (Found: C, 66·9; H, 4·6; N, 20·0; S, 9·6. $C_{20}H_{17}N_5S$ requires C, 66·8; H, 4·7; N, 19·5; S, 8·9%), was obtained similarly in 16% yield from the corresponding 2-methylamino-compound. 1 : 4-*Dihydro*-2-*mercapto*-1-*methyl*-6 : 7-*diphenyl*-4-*thionopteridine*, m. p. 375° (decomp.) (from dimethylformamide without prior extraction with sodium hydroxide) (Found: C, 63·1; H, 3·9; N, 15·3; S, 17·4. $C_{19}H_{14}N_4S_2$ requires

[5] Weijlard, Tishler, and Erickson, *J. Amer. Chem. Soc.*, 1945, **67**, 802.

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C, 63·0; H, 3·9; N, 15·5; S, 17·7%), was obtained similarly in 53% yield from 1 : 4-dihydro-2-mercapto-1-methyl-4-oxo-6 : 7-diphenylpteridine.

2-Amino-1 : 4-dihydro-4-imino-1-methyl-6 : 7-diphenylpteridine.—(*a*) 2 : 4-Diamino-6 : 7-diphenylpteridine (3 g.), methyl iodide (6 g.), and 2-ethoxyethanol (60 c.c.) were heated under reflux for 3 hr. The hydriodide which separated on cooling was collected [m. p. 315° (decomp.)] and boiled with 10% w/v sodium carbonate for 5 min., to give the base (1·7 g.) identical (m. p. and mixed m. p. 256°) with material prepared by method (*b*).

(*b*) 2-Amino-1 : 4-dihydro-1-methyl-6 : 7-diphenyl-4-thionopteridine (2 g.), yellow mercuric oxide (2·5 g.), ethanol (120 c.c.), and chloroform (20 c.c.) were heated under reflux in a stream of ammonia for 6 hr. After filtration of the hot mixture the *base* (0·9 g.) which separated on cooling was collected and crystallised from ethanol (m. p. 256°) (Found: C, 69·5; H, 4·7; N, 24·8. $C_{19}H_{16}N_6$ requires C, 69·5; H, 4·9; N, 25·6%).

2-Amino-1 : 4-dihydro-1-methyl-4-methylimino-6 : 7-diphenylpteridine, m. p. 256° (from ethanol), was obtained similarly in 21% yield (Found: C, 70·5; H, 5·8; N, 24·6. $C_{20}H_{18}N_6$ requires C, 70·2; H, 5·3; N, 24·6%).

2-Amino-3-(N-methylcarbamoyl)-5 : 6-diphenylpyrazine.—Methyl 3-amino-5 : 6-diphenylpyrazine-2-carboxylate (3·6 g.) and methylamine (50 g.) in ethanol (500 c.c.) were heated for 16 hr. at 160—170°. The *amide* which separated on cooling was collected and crystallised from methanol; it (2 g.) had m. p. 198° (Found: C, 71·0; H, 5·4; N, 18·5. $C_{18}H_{16}ON_4$ requires C, 71·1; H, 5·3; N, 18·4%).

2-Ethoxycarbamoylamino-3-(N-methylcarbamoyl)-5 : 6-diphenylpyrazine.—2-Amino-3-(*N*-methylcarbamoyl)-5 : 6-diphenylpyrazine (1·5 g.) and ethyl chloroformate (40 c.c.) were heated under reflux for 20 hr. After removal of the excess of ethyl chloroformate under reduced pressure, the *urethane* (1·7 g.), m. p. 153°, was obtained by crystallisation of the residue from chloroform–light petroleum (Found: C, 67·2; H, 5·4; N, 15·3. $C_{21}H_{20}O_3N_4$ requires C, 67·1; H, 5·3; N, 14·9%).

3 : 4-Dihydro-2-hydroxy-3-methyl-4-oxo-6 : 7-diphenylpteridine.—2-Ethoxycarbamoylamino-3-(*N*-methylcarbamoyl)-5 : 6-diphenylpyrazine (1·25 g.) was heated under reflux for 10 hr. with a solution of sodium ethoxide [from sodium (1·5 g.) in ethanol (200 c.c.)]. The residue obtained after removal of the solvent under reduced pressure was suspended in water and acidified with acetic acid; the *pteridine*, crystallised from ethanol, had m. p. 307° (0·7 g.) (Found: C, 69·3; H, 4·2; N, 16·5. $C_{19}H_{14}O_2N_4$ requires C, 69·1; H, 4·3; N, 16·9%).

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413. *Solubility of Some Polonium Compounds.*

By K. W. BAGNALL and J. H. FREEMAN.

The dependence of the solubility of polonium hydroxide on hydroxyl-ion concentration indicates that this compound is only feebly acidic; the solubilities of polonium acetate and cyanide have been determined for a wide concentration range of acetic acid and potassium cyanide respectively and some observations made on a formate, oxalate, and tartrate.

Polonium Hydroxide.—Papers on the tracer solution chemistry of polonium have indicated that this compound was acidic and analogous to tellurous acid.[1] Since our reported[2] value of 75 μg. (of ^{210}Po)/litre for the solubility of this compound in water or excess of alkali appeared to be much larger than the values suggested by the tracer work, we have investigated the dependence of the solubility in potassium hydroxide solution in the concentration range 0·26—1·73N.

[1] Haissinsky, *J. Chim. phys.*, 1932, **29**, 453; Paneth and Benjamin, *Z. Elektrochem.*, 1925, **31**, 572; Haissinsky, *Compt. rend.*, 1932, **194**, 275, 1917; Blau and Rona, *Sitzungsber. Akad. Wiss. Wien, Abt. IIa*, 1930, **139**, 275; Guillot, *Compt. rend.*, 1930, **190**, 1553.

[2] Bagnall, D'Eye, and Freeman, *J.*, 1955, 2320.

The solubility in alkali slowly increases for 24 hr. and then remains constant, even for 5 days. The addition of hydrogen peroxide does not affect the solubility.

In our determinations, the equilibrium was approached from both higher and lower concentrations of alkali; the results were consistent to $\pm 1\%$. The plot of log [KOH] against log [solubility] is linear and of slope close to 2; activity corrections were not applied. The reaction involved is probably $PoO(OH)_2 + 2KOH \rightleftharpoons K_2PoO_3 + 2H_2O$ for which the equilibrium constant

$$K_c = [K_2PoO_3]/[KOH]^2 = (8{\cdot}2 \pm 0{\cdot}4) \times 10^{-5}$$

However, one would not expect the reaction to be slow, and it is probable that other factors are involved.

Polonium hydroxide is therefore much less acidic than tellurous acid and, like the latter, its solubility in aqueous ammonia (*d* 0·88) is little different from its solubility in water (0·06 curie/l.).

Polonium Salts of Weak Acids.—These solubility determinations were part of a search for a suitable solvent for electrodeposition of polonium; nitric acid is normally used but polonium has a low solubility in this medium.

The salts described are formed as white crystals from solid polonium tetrachloride or hydroxide and an aqueous solution of the appropriate acid. Analyses were not possible owing to the rapid radiation decomposition of the solid phase after its removal from the acid solution.

Polonium acetate. The solubility in acetic acid increases from 0·88 curie/l. in 0·1N-acid to 375 curies/l. in 2N-acid, indicating complex-ion formation. The plot of log $[CH_3{\cdot}CO_2H]$ against log [solubility] is approximately linear and of slope close to 2; the plot of log $[CH_3{\cdot}CO_2^-]$ against log [solubility] has slope close to 4. The nature of the ion concerned is unknown, but the acetate complex appears to be more stable than the hexachloropolonite ion since the yellow colour characteristic of the latter does not appear when solutions of the acetate complex are acidified with hydrochloric acid.

The electrodeposits of polonium on gold prepared from solutions in acetic acid are bright and metallic and the deposition efficiency compares favourably with that from N-nitric acid. Unfortunately, comparatively large amounts of the polonium disappeared during the plating process in spite of careful trapping of the vapours emerging from the solution. Since the solution rapidly discoloured during the deposition, the losses of polonium may result from the formation of a volatile methylpolonium formed by the reaction of the elementary polonium on the electrode with free-radicals liberated in the solution, or at the electrode, by the intense α-bombardment.

Similarly, use of trichloroacetic acid is objectionable since free chlorine appears to be liberated by the α-bombardment when curie amounts of ^{210}Po are involved.

Acetic acid, might, however, be useful as a solvent for the preparation of milligram sources of the longer-lived polonium isotopes (^{208}Po and ^{209}Po), where the radiation intensity would be much less.

Polonium cyanide. The solid discolours within a few hours, even in contact with excess of potassium cyanide solution, and the salt becomes black on exposure to air. The solubility in potassium cyanide solution is low, increasing from 0·39 curie/l. in 0·05M-solution to 5·4 curies/l. in 1·5M-solution; some formation of complex ions may occur.

Polonium "formate." A black precipitate of uncertain composition and low solubility is formed by treating polonium "hydroxide" with 2N-formic acid.

Polonium "oxalate." Solubility studies with a wide concentration range of oxalic acid gave completely irreproducible results; the curve may be similar in form to the solubility curve of the polonium sulphates.[3]

Polonium "tartrate." Polonium tetrachloride is very soluble in 2N-tartaric acid,

[3] Bagnall and Freeman, *J.*, 1956, 4579.

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giving a colourless solution which slowly becomes grey. Electrolysis of this solution between gold electrodes led to the deposition of 12% of the polonium on the cathode and 65% on the anode; the remainder was not deposited; both electrodes became covered with a layer of carbon, presumably from the radiation decomposition of the tartaric acid.

Experimental.—All the work was carried out in glove-boxes in order to minimise the hazards associated with the handling of high levels of α-activity.

The techniques used for the solubility determinations have been described.[3,4]

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[*Received, December 13th,* 1956.]

[4] Bagnall, D'Eye, and Freeman, *J.*, 1956, 3385.

414. *The Latent Heats of Vaporization of the Alkyl Nitrates.*

By PETER GRAY and M. W. T. PRATT.

The vapour pressures of *n*- and *iso*-propyl and *n*- and *iso*-butyl nitrate have been measured from 0° to 70°, and their normal b. p.s have been remeasured. From these results accurate values are derived for the latent heats of vaporization of the nitrates at 25° and at their boiling points by means of the Clausius–Clapeyron equation. Corrections for gas imperfection and finite liquid volume are applied to this equation, and previously existing latent-heat determinations for methyl and ethyl nitrate are also corrected. The following values (kcal. mole^{-1}) for ΔH_v at 25° have been found for the alkyl nitrates: Me 8·15; Et 8·67; Pr^n 9·70; Pr^i 9·27; Bu^n 10·42; Bu^i 10·08. Latent heats at the b. p. are also recorded; all the Trouton "constants" (cal. deg.$^{-1}$ mole^{-1}) are about 22·5 ± 0·5. The variation with temperature of latent heat indicates that at room temperature fewer than half the possible vibrational modes are active in the gaseous nitrates.

THE latent heats of vaporization of only three alkyl nitrates have been measured.[1] McKinley-McKee and Moelwyn-Hughes [2] measured the vapour pressure of methyl nitrate over a range of temperature and deduced the latent heat of vaporization as 7·728 kcal. mole^{-1} at 64·6°, the normal boiling point. They did not correct their results for gas imperfections and this value needs revision. The vapour pressure of ethyl nitrate has been measured at moderate,[3] low,[4] and high [5] temperatures and its latent heat of vaporization found [3] to be ~8·7 kcal. mole^{-1} at 25°. An empirical equation for the vapour pressure of *iso*propyl nitrate is also available.[6]

The importance of such latent heat information was shown in a previous paper [3] in which a new measurement of the latent heat of vaporization of ethyl nitrate was used to deduce the best values for the standard enthalpies of formation of liquid and gaseous ethyl nitrate. The results chosen on this basis as the best available—enthalpy of formation at 25° of liquid ethyl nitrate, −45·7 kcal. mole^{-1}, and of gaseous ethyl nitrate, −37·0 kcal. mole^{-1}—have now been substantiated by Skinner and Fairbrother,[7] who from the heat of combustion, showed that the enthalpy of formation of liquid ethyl nitrate is −45·51 ± 0·25 kcal. mole^{-1}.

We have now measured the vapour pressures of *n*- and *iso*-propyl and *n*- and *iso*-butyl nitrate over the range 0—70°, and have remeasured their normal boiling points, as the literature values are discordant. Empirical equations relating vapour pressure and

[1] Gray and Pratt, XXVIII Congr. Ind. Chem., Madrid, 1955.
[2] McKinley-McKee and Moelwyn-Hughes, *Trans. Faraday Soc.*, 1952, **48**, 247.
[3] Gray, Pratt, and Larkin, *J.*, 1956, 210.
[4] Goodeve, *Trans. Faraday Soc.*, 1934, **30**, 501.
[5] Hildenbrand and Whittaker, *J. Phys. Chem.*, 1955, **59**, 1024.
[6] Technical Data Sheet, Ethyl Corp., Detroit.
[7] Skinner and Fairbrother, personal communication.

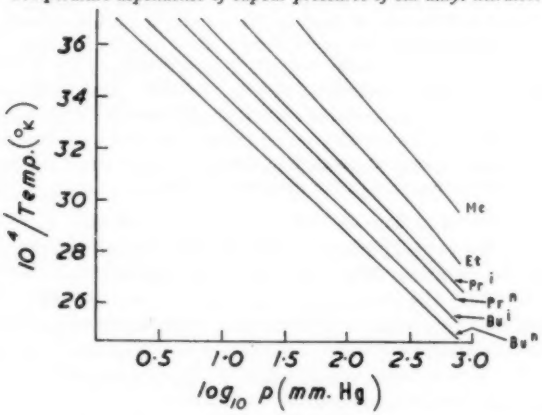
temperature (Antoine equations) which are also satisfied by the normal boiling points have been fitted to the experimental results. The latent heats of vaporization of the four nitrates at 25° and at their boiling points have been derived from the Antoine equations by means of the Clausius–Clapeyron equation; corrections have been applied for non-ideal gas behaviour and for finite liquid volume.

In what follows we use the symbolism in the annexed Table.

a, A, b, B, D, X, Y	Arbitrary constants
C_p (cal. deg.$^{-1}$ mole^{-1})	Molar specific heat at constant pressure
δ	Fractional error involved in using approx. form of the Clausius–Clapeyron eqn.
M	Mol. wt.
n	No. of atoms in a molecule
p (mm. Hg)	Saturation v. p. at $t°$ c
ρ_l (g. cm.$^{-3}$)	Density of liquid at $t°$ c
t (° c), T (° k)	Temperature
T_b (° k)	B. p.
T_c (° k)	Critical temp.
V_c (cm.^{3} mole^{-1})	Critical volume
V_g (cm.^{3} mole^{-1})	Volume of 1 mole of gas at $T°$ and p mm. pressure
V_l (cm.^{3} mole^{-1})	Volume of 1 mole of liquid at $T°$ and p mm. pressure

Empirical Vapour-pressure Equations.—Plots of $\log_{10} p$ against $1/T$ are shown in the Figure for the propyl and butyl nitrates, with, for comparison, the vapour-pressure curves

Temperature dependence of vapour pressures of six alkyl nitrates.



of methyl [2] and ethyl nitrate.[3] The curves depart only very slightly from straight lines in the range 0—70° c. B. p. data for the higher nitrates show that curvature increases at higher temperature. This non-linearity indicates departure from the approximate relation $\log p = A + B/T$, and the vapour pressure results are fitted to the Antoine equation $\log_{10} p = A - B/(t + D)$ which has three empirical constants instead of two. The

TABLE 1. *Vapour-pressure equations,* $\log_{10} p$ (*mm.* Hg) $= A - B/(t + D)$.*

Nitrate	*A*	*B*	*D*	Nitrate	*A*	*B*	*D*
Ethyl	7·145	1329	224·0°	*n*-Butyl	7·607	1742	235·6°
n-Propyl	7·246	1444	220·8	*iso*Butyl	7·424	1597	228·6
*iso*Propyl	7·303	1457	227·5				

* For methyl nitrate the alternative equation:
$\log_{10} p$ (mm. Hg) $= 26{\cdot}6767 - 6{\cdot}3431 \log_{10} T - 2620{\cdot}1139/T$ has been fitted successfully [2] to the experimental data.

constants of the Antoine equations which best fit all the available vapour-pressure and normal boiling-point data are listed in Table 1, and in Table 2 the experimentally measured vapour pressures are compared with those calculated from the appropriate empirical

equation. The vapour pressure curve of normal propyl nitrate is close to that found by the Ethyl Corporation,[6] who give the relation $\log_{10} p = 7{\cdot}3506 - 1520/(t + 230)$.

TABLE 2. *Experimental vapour pressures ($p_{exp.}$, mm. Hg), compared with calculated vapour pressures ($p_{calc.}$) derived from the relations given in Table 1.*

	Ethyl		*n*-Propyl		*iso*Propyl		*n*-Butyl		*iso*Butyl	
Temp. (° c)	$p_{exp.}$	$p_{calc.}$	$p_{exp.}$	$p_{calc.}$	$p_{exp.}$	$p_{calc.}$	$p_{exp.}$	$p_{calc.}$	$p_{exp.}$	$p_{calc.}$
0	16·1	16·3	5·3	5·1	7·3	7·9	1·7	1·7	2·9	2·7
10	29·4	29·2	10·0	9·8	14·6	14·7	3·3	3·3	5·4	5·4
20	49·5	49·9	17·8	17·7	26·5	26·1	6·3	6·2	10·0	10·0
30	81·5	81·8	30·6	30·8	44·5	44·2	11·1	11·2	17·8	17·7
40	128	129	50·7	51·2	72·1	71·8	18·9	19·3	30·1	30·1
50	198	197	81·4	81·8	113	113	32·1	32·1	48·5	49·0
60	293	292	128	127	172	172	51·8	51·8	77·9	77·8
70	420	422	189	190	256	255	81·1	80·7	120	119
B. p.	760	760	760	760	760	760	760	760	760	760

Latent Heats of Vaporization.—The Clausius–Clapeyron equation is used to derive latent heats of vaporization from the vapour-pressure equations :

$$\Delta H_v = T(V_g - V_l)(\mathrm{d}p/\mathrm{d}T)_{sat.} \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (1)$$

An approximate form of this is :

$$(\mathrm{d} \ln p/\mathrm{d}T)_{sat.} = \Delta H_v/\boldsymbol{R}T^2 \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (2)$$

The fractional error δ involved in using eqn. (2) instead of the exact form (1) is estimated as follows. From eqn. (1) :

$$\Delta H_v/\boldsymbol{R}T^2(\mathrm{d} \ln p/\mathrm{d}T) = p(V_g - V_l)/\boldsymbol{R}T = 1 - \delta$$

The assumptions in eqn. (2) are that $V_l = 0$, and that $pV_g = \boldsymbol{R}T$. The fractional error δ is therefore made up of a contribution due to the finite volume of the liquid, δ_l, and a contribution due to gas imperfection, δ_g, *i.e.*, $\delta = \delta_g + \delta_l$.

Correction for Finite Liquid Volume.—δ_l is the fractional error in replacing $p(V_g - V_l)/\boldsymbol{R}T$ by $pV_g/\boldsymbol{R}T$.

Therefore $\delta_l = pV_l/\boldsymbol{R}T \simeq V_l/V_g$

Now $V_l = M/\rho_l$

Therefore $$\delta_l = \frac{M}{\rho_1} \cdot \frac{p}{760} \cdot \frac{273}{T} \cdot \frac{1}{22{,}400}$$

Correction for Gas Imperfection.—δ_g is the fractional error due to assuming $pV_g = \boldsymbol{R}T$, *i.e.*, $\delta_g = 1 - (pV_g/\boldsymbol{R}T)$. We may derive an expression for δ_g, in terms of the critical constants V_c and T_c, from the Berthelot equation :

$$(p + a/TV_g^2)(V_g - b) = \boldsymbol{R}T$$

$$pV_g/\boldsymbol{R}T = 1 + b/V_g - a/\boldsymbol{R}T^2V_g$$

Therefore $$\delta_g = (a/\boldsymbol{R}T^2 - b)/V_g$$

Setting $a/\boldsymbol{R}T^2 = 3V_cT_c^2/2T^2$, and $b = V_c/4$, the values adopted [8] by D. Berthelot and found satisfactory for organic vapours by Lambert *et al.*,[9] we have :

$$\delta_g = \frac{V_c}{V_g}\left(\frac{3T_c^2}{2T^2} - \frac{1}{4}\right)$$

Alkyl nitrates are all dangerously explosive and since, as far as we are aware, their critical temperatures and critical volumes have never been measured the approximations

[8] Partington, "An Advanced Treatise on Physical Chemistry," Vol. I, Longmans, Green and Co., London, 1949, p. 650.

[9] Lambert, Roberts, Rowlinson, and Wilkinson, *Proc. Roy. Soc.*, 1949, *A*, **196**, 113.

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$T_c \simeq 1{\cdot}5T_b$ (Guldberg's rule) and $V_c \simeq 3V_l$ (Partington [8]) have been used. To this degree of accuracy:

$$\delta_g = \frac{V_l}{V_g}\left(\frac{81}{8} \cdot \frac{T_b^2}{T^2} - \frac{3}{4}\right)$$

In this equation, V_g may be replaced by its ideal value, $V_g = 22{,}400(T/273)(760/p)$. The approximations involved in the derivations of δ_l and δ_g introduce only minor errors into the latent heats themselves.

In previous work [2-4] the Clausius–Clapeyron eqn. (2) has been used without corrections for the assumptions involved. The opportunity is now taken of correcting the former values of the latent heats of vaporization of methyl and ethyl nitrates at their boiling points.

TABLE 3. *Latent heats and entropies of vaporization of the alkyl nitrates.*

	25°c					Boiling point					
Nitrate	$RT^2\frac{d\ln p}{dT}$ (cal. (mole^{-1})	$10^3\delta_l$	$10^3\delta_g$	$10^3\delta$	Corr. ΔH_v (cal. mole^{-1})	$RT^2\frac{d\ln p}{dT}$ (cal. mole^{-1})	$10^3\delta_l$	$10^3\delta_g$	$10^3\delta$	Corr. ΔH_v (cal. mole^{-1})	Entropy of vapn. (cal. deg.$^{-1}$ mole^{-1})
Methyl ...	8230	0·5	8·0	8·5	8150	7730	2·4	22·6	25·0	7540	22·3
Ethyl ...	8720	0·3	4·4	4·7	8670	8150	2·9	25·8	28·7	7920	21·9
n-Propyl	9720	0·1	2·3	2·4	9700	8870	3·3	31·0	34·3	8580	22·3
*iso*Propyl	9300	0·2	3·1	3·3	9270	8640	3·4	31·8	35·2	8350	22·2
n-Butyl ...	10,430	0·0	0·9	0·9	10,420	9680	3·6	33·7	37·3	9340	23·1
*iso*Butyl	10,100	0·1	1·5	1·6	10,080	9280	3·8	36·2	40·0	8920	22·7

In Table 3 the corrected and the uncorrected latent heats of vaporization of the six alkyl nitrates are listed, for 25° c and the normal boiling points. The latent-heat values derived here at 25° are the more precise for two reasons. First, the experimental points in this region are more numerous and more precise than near the boiling point. Secondly, at 25° the correction δ is in all cases less than 1·0%; it is least for the least volatile nitrates. At the boiling point the correction is 2—5% and is least for the most volatile nitrates. For this reason when the Clausius–Clapeyron equation is used in its simplified form (2) to derive latent heats at the boiling point there is usually no justification in quoting ΔH_v to more than two significant figures. Very precise equation of state data are needed to obtain values of ΔH_v accurate to ± 5 cal. mole^{-1}. An interesting instance where these complete data are available is provided by nitromethane.[10]

Entropies of Vaporization.—The standard entropies of vaporization at the boiling points (Trouton's "constants") (see Table 3) lie in the range $22{\cdot}5 \pm 0{\cdot}6$ cal. deg.$^{-1}$ mole^{-1}, indicating that the liquid nitrates are not associated. As the Trouton's "constant" increases only slightly as the series is ascended, the latent heat of higher nitrates may be safely estimated by assuming a Trouton's "constant" of about 23 cal. deg.$^{-1}$ mole^{-1}.

Variation in Latent Heat with Temperature and the Specific Heats in Liquid and Vapour Phases.—Our results for the variation with temperature of the latent heat of vaporization fit, to a first approximation, the equation $\Delta H_v = X - Y(t - 25)$, the calculated values of X and Y being shown in Table 4. Application of the equation $d\Delta H_v/dT \simeq C_p(\text{gas}) - C_p(\text{liquid})$ yields * the values for $C_p(\text{gas}) - C_p(\text{liquid})$ in Table 4. The specific heats of liquid methyl [11] and ethyl nitrates [13] have been measured at 25°. For the other nitrates C_p(liquid) has been estimated by multiplying the molecular weight by the factor

* The exact form of this equation is:

$$d\Delta H_v/dT = \Delta C_p + L/T - L(d\ln \Delta V/dT)_p$$

For the transition liquid ⟶ gas the second and the third term of this expression are very nearly equal.

[10] McCullough, Scott, Pennington, Hossenlopp, and Waddington, *J. Amer. Chem. Soc.*, 1954, **76**, 4791, and references cited therein.
[11] Gray and Smith, *J.*, 1953, 2380.

0·44. (Experimentally the factor is 0·49 for methyl nitrate, and 0·45 for ethyl nitrate.) Hence C_p(gas) may be estimated.

TABLE 4. *Implications of temperature-dependence of latent heat of vaporization,* ΔH_v *(cal. mole*$^{-1}$*)* $= X - Y(t - 25)$,* *where* X *= latent heat of vaporization (cal. mole*$^{-1}$*) at 25°, and* $Y \simeq$ *specific heat decrement (cal. deg.*$^{-1}$ *mole*$^{-1}$*) on vaporization. (Entries, except in the last column, are in cal. deg.*$^{-1}$ *mole*$^{-1}$*.)*

Nitrate	Y	C_p(liq)	C_p(gas)	C_p(gas) due to internal vibrations (approx.)	C_p(gas) if all $(3n - 6)$ vibrations active (approx.)	Fraction of vibrations active at *ca.* 25° c (approx.)
Methyl	15·7	37·6	22	14	36	0·39
Ethyl	10·3	40·7	30	22	54	0·40
n-Propyl	13·2	46	33	25	72	0·35
*iso*Propyl.....	11·9	46	34	26	72	0·36
n-Butyl	9·8	52	42	34	90	0·38
*iso*Butyl	11·8	52	40	32	90	0·36

* For ethyl nitrate, valid from − 30° to 110°; for other nitrates from 25° to the normal b. p.

Fraction of Vibrations Active.—The value of the specific heat of the vapour derived above may be used to estimate the fraction of the possible vibrational modes of the nitrates which are active at room temperature.

The contribution to the specific heat of the gas made by the internal motions of the molecule (vibrations, and internal rotations) is C_p(gas) $- 4\boldsymbol{R}$: the term $4\boldsymbol{R}$ is made up of $3\boldsymbol{R}/2$ for translation, $3\boldsymbol{R}/2$ for rotation of the molecule as a whole, and $\boldsymbol{R}$ to convert the specific heat from constant-pressure into constant-volume conditions.

The nitrate molecules are non-linear, so that if all possible vibrations were active, they would contribute $(3n - 6)\boldsymbol{R}$ cal. deg.$^{-1}$ mole^{-1} to the specific heat. Table 4 shows that the contribution made to the specific heat by the internal rotations varies from 35 to 40% of the maximum possible, so that fewer than half the vibrations of the gaseous alkyl nitrates are active at room temperature and the fraction of active vibrations decreases slowly as the series is ascended.

EXPERIMENTAL

Materials.—*n*- and *iso*-Propyl and *n*- and *iso*-butyl nitrate were prepared by fractionating the corresponding alcohols, and adding 35 ml. very slowly from a tap funnel to an ice-cooled mixture of 50 ml. each of concentrated sulphuric and nitric acid. The mixture was vigorously stirred, and the temperature kept below 3°. The ester was decanted, washed immediately with sodium carbonate solution and water, dried ($CaCl_2$), and fractionated under reduced pressure. Physical constants of the purified nitrates are shown in Table 5.

TABLE 5.

Nitrate	B. p./760 mm.	d^{20}	n_D^{20}	Nitrate	B. p./760 mm.	d^{20}	n_D^{20}
Methyl	64·6°	1·205	1·3748	*iso*Propyl.....	102°	1·05	1·3913
Ethyl	87·7	1·12	1·3857	*n*-Butyl	133	1·03	1·4069
n-Propyl	110	1·06	1·3980	*iso*Butyl	123	1·02	1·4026

The b. p. of *n*-propyl nitrate, which is much higher than the figure (100·5°) quoted by the International Critical Tables,[12] is in agreement with that deduced from the vapour-pressure data of the Ethyl Corporation,[6] and the b. p. given by Wheeler, Whittaker, and Pike.[14] The b. p. of *n*-butyl nitrate, 133°, is 3° lower than that in International Critical Tables;[12] those of *iso*propyl and *iso*butyl nitrate are identical with recorded values.[13]

Apparatus and Method.—The vapour pressures were measured over the range 0—70° at approximately 5° intervals in standard apparatus in which a bulb containing the liquid nitrate was connected to a wide-bore (12 mm.) mercury manometer. The apparatus was immersed in

[12] Internat. Crit. Tables, McGraw-Hill Book Co., New York, 1927.
[13] Gray and Smith, *J.*, 1954, 769.
[14] Wheeler, Whittaker, and Pike, *J. Inst. Fuel*, 1947, **20**, 137.

a thermostat. The height of the mercury was measured by a cathetometer, and allowance made for the variation in density of the mercury with temperature. Several samples of each nitrate were used and, to check the purity of the liquid nitrate, the vapour pressure of the last drop left in the apparatus was compared with that of the original volume at the same temperature. The identity of these pressures showed that no fractionation had occurred; the composition of the last drop was the same as that of the bulk.

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415. *Hydrolysis of the Uranyl Ion.*

By J. A. HEARNE and A. G. WHITE.

The pH of uranyl perchlorate solutions has been measured over a wide concentration range at various temperatures and ionic strengths. The results can be explained in terms of two hydrolytic reactions, leading respectively to the formation of the monomeric $UO_2 \cdot OH^+$ and the dimeric $UO_2 \cdot UO_3^{2+}$ ion, ΔH for formation of the former being considerably larger than for the latter. The effect of complex formation with anions is discussed and a new method of detecting perchlorate-complex formation is suggested.

THE hydrolysis of uranyl salts has been investigated several times (for a survey see Kraus [1]). The problem is complex and the work of Sutton [2] and of Ahrland [3] leaves little doubt that in solutions containing added alkali or an excess of uranium trioxide polymeric species containing three or more uranium atoms occur. The species existing in stoicheiometric uranyl salt solutions however are less certain. The work of Singh and Ahmad [4] on the pH of uranyl nitrate, sulphate, and acetate solutions does not permit a detailed analysis as no attempt was made to control the ionic strength. The same criticism also applies to the much-quoted work of Longsworth and MacInnes,[5] although they attempted to interpret their results in terms of various possible hydrolytic equilibria and obtained a fair agreement with experiment over a moderate concentration range by means of the single reaction :

$$2UO_2^{2+} + H_2O \rightleftharpoons UO_2 \cdot UO_3^{2+} + 2H^+ \quad . \quad . \quad . \quad . \quad . \quad (1)$$

Guiter's measurements [6] on uranyl nitrate solutions purported to show the existence of species such as $UO_2 \cdot OH,NO_3$, and $UO_2 \cdot OH(NO_3^-)_2$, in addition to $UO_2 \cdot UO_3^{2+}$. The pH measurements however were made colorimetrically, neither temperature nor ionic strength was controlled, and the analysis given involves some doubtful assumptions. In Faucherre's very careful work,[7] however, both ionic strength and temperature were controlled and the conclusion reached was that the hydrolysis could in fact be explained entirely on the basis of reaction (1); this investigation was carried out on uranyl nitrate in barium nitrate solution and as it has been demonstrated that the nitrate ion forms a complex with the uranyl ion [8,9] it is clear that the hydrolytic constants given by Faucherre [7] may contain a factor dependent on this effect.

[1] Kraus, Proc. Internat. Conference on the Peaceful Uses of Atomic Energy, Vol. VII,, p. 245, United Nations, N.Y., 1956.
[2] Sutton, Nat. Res. Council, Canada Atomic Energy Project, Report CRC 325 (1947); *J.*, 1949, S 275.
[3] Ahrland, *Acta. Chem. Scand.*, 1949, **3**, 374; 1954, **8**, 1907.
[4] Singh and Ahmad, *J. Chim. phys.*, 1937, **34**, 351.
[5] Longsworth and MacInnes, U.S.A.E.C. Report MDDC 911 (1947).
[6] Guiter, *Bull. Soc. chim. France*, 1947, 64.
[7] Faucherre, *Compt. rend.*, 1948, **227**, 1367.
[8] Betts and Michels, *J.*, 1949, S 186.
[9] Ahrland, *Acta Chem. Scand.*, 1951, **5**, 1271.

So it seemed worth while to carry out measurements similar to those described by Faucherre [7] but with uranyl perchlorate in a perchlorate medium and, as all previous work has been carried out at one temperature only, to extend them to at least two temperatures.

Experimental and Results

Solutions were made up with doubly distilled water freed from carbon dioxide by the passage of nitrogen. The pH of this water was 6·95.

Uranyl perchlorate stock solutions were made by dissolving high-purity uranium trioxide, the water content of which was determined by analysis just before use, in the stoicheiometric quantity of 2M-perchloric acid and diluting the product to the required volume with water. Dissolution of the oxide required 24—48 hr. at 40—50°. Other solutions were prepared by dilution of the uranyl perchlorate stock with water and/or barium perchlorate solution. The pH of the barium perchlorate solution used for the dilutions was 7·13.

Two specimens of uranium trioxide were used, one supplied by Mr. P. C. Davidge of this Division, the other prepared by the peroxide precipitation process.[5] Results obtained with them were identical.

Pyrex glassware was used and all pH's, save those of the stock solutions, were measured as soon after making up of a given solution as possible. A check on the uranyl perchlorate stock solution revealed no change in pH during many days.

pH was measured with a Cambridge glass electrode and a Cambridge pH meter used as a valve potentiometer. The reference electrode was a calomel element containing saturated sodium chloride with a saturated sodium chloride salt bridge. This procedure was adopted to avoid the difficulties which would arise at the liquid junction, owing to precipitation, if a potassium chloride element were used.

The cell was that described by Coates,[10] modified by use of a bulb, of approx. 100 ml. capacity, as the glass electrode compartment, provision of a tap in the side arm for introduction of the solution, and addition of inlet and outlet tubes for the passage of nitrogen through the solution in the glass electrode compartment. A standard cone and socket joint was used to hold the glass electrode which was cemented in place with Apiezon W wax.

Table 1. pH *of uranyl perchlorate solutions at* 25·0°.

$UO_2(ClO_4)_2$ (10^{-3} M)	9·4	5·0	0·94	0·188	0·0376	0·0188	0·00752	0·0047	0·00188
pH	2·61	2·75	3·25	3·71	4·15	4·38	4·69	4·81	5·18

Table 2. pH *of uranyl perchlorate solutions at* 25·0°.

Stoicheiometric uranyl perchlorate.

10^{-3}M	94	11·58	9·4	1·88	0·94	0·47	0·188	0·094	0·047	0·0235
pH	2·55	3·25	3·34	3·86	4·10	4·36	4·72	4·95	5·21	5·45

Ionic strength 0·347.

10^{-3}M	115·8	11·58	2·315	0·479	0·1158	0·02315	0·0158
pH	2·45	3·15	3·61	4·09	4·49	4·98	5·22

Ionic strength 0·0347.

10^{-3}M	11·58	2·315	0·279	0·1158	0·02315
pH	3·25	3·73	4·21	4·61	5·10

Table 3. pH *of uranyl perchlorate solutions at* 40·0°.

Stoicheiometric uranyl perchlorate.

10^{-3}M	115·8	11·58	1·88	0·94	0·47	0·188	0·094	0·047	0·0188	0·0094
pH	2·38	3·19	3·79	3·97	4·27	4·58	4·87	5·07	5·45	5·73

Ionic strength 0·0347.

10^{-3}M	11·58	2·315	0·479	0·158	0·02315
pH	3·19	3·57	4·07	4·47	4·96

The entire cell assembly was immersed in a thermostatically controlled (±0·02°) oil-bath. When the bath-temperature was changed the cell was left for 24 hr. before further measurements.

The glass-electrode response was checked frequently during the measurements with 0·05M-potassium hydrogen phthalate and with 0·01M-hydrochloric acid.

[10] Coates, *J.*, 1945, 489.

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After introduction of a solution into the cell ¾—1 hr. was allowed to elapse in order to attain temperature equilibrium before the liquid junction was made and the potential measured. During this time nitrogen, saturated with water vapour at the bath-temperature, passed continuously in a rapid stream through the solution in the cell.

The only previous measurements of the pH of stoicheiometric uranyl perchlorate are those of Sutton,[2] but it is not clear whether the author took precautions to exclude carbon dioxide. To check this, measurements were carried out of the pH of stoicheiometric uranyl perchlorate solutions which had been made from ordinary distilled water and in which no nitrogen was passed through the cell. The results are given in Table 1, and when plotted are in good agreement with Sutton's results, suggesting that the latter were obtained in the presence of carbon dioxide. Further measurements were then made by the method described above, in which carbon dioxide was excluded, both of the pH of stoicheiometric uranyl perchlorate solutions and of solutions kept at constant ionic strength by the addition of barium perchlorate. The results are reported in Tables 2 and 3. A plot of the results of Table 1 together with the comparable figures from Table 2, in the form of pH against log c, reveals that failure to take adequate precautions to remove carbon dioxide has a pronounced effect which is of particular importance since in the interpretation much depends upon the slope of similar plots. It therefore appears to be a fortunate cancellation of errors that gave Longsworth and MacInnes [5] and Sutton [2] a pH—log c plot of the slope required by reaction (1) and not one indicating a quite different mechanism.

Discussion

As a starting point for the analysis of the results obtained in this investigation the method proposed by Geloso and Faucherre [11] and slightly modified by Faucherre [7] was used. These authors show that for the general hydrolytic reaction

$$n\mathrm{A}^{z+} + p\mathrm{H_2O} \rightleftharpoons \alpha_n^{y+} + q\mathrm{H}^+$$

where α_n^{y+} is the n-meric hydrolysis product, the hydrogen-ion concentration and the total metal concentration $[\mathrm{A}]_T$ are related by the expression :

$$\log [\mathrm{H}^+] = \frac{n}{q+1} \log ([\mathrm{A}]_T - [\mathrm{H}^+]) + \frac{1}{q+1} \log Kq \quad . \quad . \quad . \quad (2)$$

[It should be noted that the original authors replaced Kq in the final term of eqn. (2) with a combined constant k.] The slope of a plot of pH against log $([\mathrm{A}]_T - [\mathrm{H}^+])$, thus provides, n and q being assumed equal, a measure of the number of metal ions taking part in the reaction, while the intercept yields a value for the hydrolysis constant K.

Our results, for the series carried out at constant ionic strength, plotted in this way, lie on straight lines, as required by eqn. (2), while those for the stoicheiometric solutions give curves. Change of ionic strength markedly affects K, as expected, and it is presumably this effect which produces the curvature in the plots for stoicheiometric solutions. It is important to note that the plots for the stoicheiometric solutions are rather misleading as, over more limited concentration ranges, they are approximately linear. In the present case, for example, a line of slope 0·8 could be drawn through many of the points apparently indicating a value of 4 for n, *i.e.*, the formation of a tetrameric hydrolysis product. When attention is confined to the results at constant ionic strength the slopes of the best straight lines, determined by the method of least squares, are : at 25°, 0·646 for ionic strength $\mu = 0{\cdot}347$, and 0·646 for $\mu = 0{\cdot}0347$; at 40°, 0·607 for $\mu = 0{\cdot}0347$; this indicates a very different state of affairs.

The difference in the slope from the value of 0·67 found by Faucherre,[7] and expected if reaction (1) is the sole hydrolytic process, is susceptible of two explanations : one, the least probable, is that n and q differ; the other that in addition to reaction (1) the equilibrium,

$$\mathrm{UO_2^{++}} + \mathrm{H_2O} \rightleftharpoons \mathrm{UO_2{\cdot}OH^+} + \mathrm{H^+} \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (3)$$

[11] Geloso and Faucherre, *Compt. rend.*, 1948, **227**, 200.

also occurs to a small extent. Komar and Tretyak [12] claim to have demonstrated that (3) is the sole hydrolytic reaction in slightly acidified solutions of uranyl nitrate; however, only a very narrow concentration range was covered and no attempt was made to work at constant ionic strength; their claim cannot, without further evidence, be regarded as valid. Neither can Harris and Kolthoff [13] be considered to have proved the existence of $UO_2{\cdot}OH^+$; their pH measurements, on uranyl chloride, were made with the quinhydrone electrode and are all very much lower than those of Longsworth and MacInnes,[5] suggesting that the solutions contained excess of acid. The hydrolysis "constant" which they calculated is based on a number of very dubious assumptions concerning activity coefficients.

If we assume that the hydrolytic processes occurring under the conditions of the present work are represented by reactions (1) and (3) and write

$$K_1 = [UO_2{\cdot}OH^+][H^+]/[UO_2^{2+}] \text{ and } K_2 = [UO_2{\cdot}UO_3^{2+}][H^+]^2/[UO_2^{2+}]^2$$

then, by combination with the conditions that

$$[U_T] = [UO_2^{2+}] + [UO_2{\cdot}OH^+] + 2[UO_2{\cdot}UO_3^{2+}]$$

and

$$[U]_T = [UO_2^{2+}] + [H^+]$$

where $[U_T]$ is the total analytical uranium concentration, it follows that

$$[U_T] = ([U_T] - [H^+])\left\{1 + \frac{K_1}{[H^+]} + \frac{2K_2([U_T] - [H^+])}{[H^+]^2}\right\} \quad . \quad . \quad . \quad (4)$$

For testing the experimental data rearrangement of eqn. (4) to the form (5) is more

$$\left\{\frac{[U_T]}{[U_T] - [H^+]} - 1\right\}[H^+] = K_1 + 2K_2\left(\frac{[U_T]}{[H^+]} - 1\right) \quad . \quad . \quad . \quad . \quad (5)$$

satisfactory. In the attached Figure the function on the left-hand side of eqn. (5) has been plotted against $([U_T]/[H^+] - 1)$ for the three sets of measurements made at constant ionic strength, and in each case there is a linear relation and a non-zero intercept, as is required if eqn. (5) and the assumptions upon which it rests represent the processes essentially correctly. From the slopes and intercepts of these plots values have been calculated for K_1 and K_2 which are given in Table 4.

TABLE 4.

Temp.	25·0°		40·0°
μ	0·347	0·0347	0·0347
10^6K_1	4	1·5	8
10^6K_2	1·5	0·7	1·2

Before considering these values it is necessary to examine the various assumptions which are implicit in their calculation. The most important is that in a medium of constant ionic strength all activity coefficients may be regarded as constant and included in the measured values of K_1 and K_2, so that:

$$K_1 = K_{01} \cdot \gamma_{UO_2^{2+}}/\gamma_{UO_2{\cdot}OH^+}\gamma_{H^+} \text{ and } K_2 = K_{02} \cdot \gamma^2_{UO_2^{2+}}/\gamma_{UO_2{\cdot}UO_3^{2+}}\gamma^2_{H^+}$$

where K_{01} and K_{02} are the true thermodynamic hydrolysis constants. For the hydrogen ion the concentration of which is always very low and which is present in only small quantities relatively to the total ion concentration, this is probably nearly true, but it is speculative whether this is also the case for the uranyl ion and its hydrolysis products in a medium varying from pure uranyl perchlorate to barium perchlorate containing a

[12] Komar and Tretyak, *Zhur. analit. Khim.*, 1955, **10**, 236.
[13] Harris and Kolthoff, *J. Amer. Chem. Soc.*, 1947, **69**, 446.

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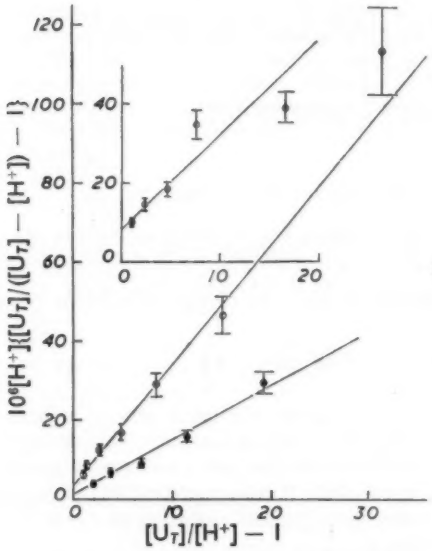
small amount of the uranyl salt. If the activity coefficients of the uranium species should vary with the barium : uranium ratio of the medium, then possibly K_1 and certainly K_2 would also vary with this ratio, making eqn. (5) non-linear. The experimental results show that eqn. (5) is approximately linear, so that the effect, if it occurs, cannot be large. However, a satisfactory resolution of this point cannot be achieved without either results of much higher precision or, preferably, an independent determination of the requisite activity coefficients. The other important assumption is that in view of the very low concentrations involved the value of γ_{H^+} can be set equal to unity, permitting the use of the simplification $pH = -\log_{10}[H^+]$.

The derivation of eqn. (5) also assumes (*a*) that there is no complex formation between the uranyl ion and perchlorate ion or (*b*) that, if such complex formation occurs, the uranyl



Plot of data according to eqn. (5).

○, $\mu = 0{\cdot}347$. ●, $\mu = 0{\cdot}0347$. Temp. = 25·0°.

Inset: ○, $\mu = 0{\cdot}0347$. Temp. = 40·0° Vertical and horizontal lines indicate the effects of errors of 0·02 unit of pH.

ions possess identical hydrolysis constants whether engaged in complexes or not. Attempts to detect such complex-ion formation have so far failed (cf., *e.g.*, Betts and Michels [8]), but it cannot be ruled out. The alternative supposition (*b*) is most unlikely to be valid, as may be seen by comparison of the present results with those of Faucherre.[7] Faucherre, working with nitrate solutions, found the value of K_2 to increase with a decrease in ionic strength, whereas the results given above show that in perchlorate solutions K_2 decreases with a decrease in ionic strength. If the changes in activity coefficients with concentration are comparable in nitrate and perchlorate solution this difference can be explained in terms of the formation of $UO_2{\cdot}NO_3^+$ complex ions, which is known to occur [8,9] in nitrate solutions, only if these ions either are not hydrolysed or have a very much smaller hydrolysis constant than the uranyl ion has. In Faucherre's work a decrease in ionic strength implies also a decrease in the total nitrate concentration and hence a decrease in the extent of complex formation by the nitrate ion, thus leaving more uranyl ion free for hydrolysis, *i.e.*, apparently increasing the hydrolysis constant.

The problem of competition between complex-ion formation and hydrolysis is worth examining in more detail. Consider the case of the perchlorate and assume that in addition to the two reactions (1) and (3) the equilibrium (6) also occurs :

$$UO_2^{2+} + ClO_4^- \rightleftharpoons UO_2{\cdot}ClO_4^+ \quad . \quad . \quad . \quad . \quad . \quad . \quad (6)$$

with $K_c = [UO_2{\cdot}ClO_4^+]/[UO_2^{2+}][ClO_4^-]$. Combination with K_1 and K_2 and the new conditions that

$$[U_T] = [UO_2^{2+}] + [UO_2{\cdot}OH^+] + 2[UO_2{\cdot}UO_3^{2+}] + [UO_2{\cdot}ClO_4^+]$$

and $$[U_T] = [UO_2^{2+}] + [UO_2{\cdot}ClO_4^+] + [H^+]$$

leads, for conditions under which it is permissible to write $[ClO_4^-] = [ClO_4]_T$, the latter being the total perchlorate concentration, to the expression (7):

$$\left\{\frac{[U_T]}{[U_T] - [H^+]} - 1\right\}[H^+] = \frac{K_1}{(1 + K_c[ClO_4]_T)} + \frac{2K_2}{(1 + K_c[ClO_4]_T)^2}\left(\frac{[U_T]}{[H^+]} - 1\right) \quad (7)$$

Comparison of eqns. (5) and (7) reveals that complex-ion formation will not modify the conclusions regarding the mechanism of hydrolysis but that the constants will differ from the true hydrolysis constants K_1 and K_2.

Equation (7) is not restricted solely to the perchlorate ion as the derivation is valid for any complex ion of the type UO_2X^+. Hence by combination of hydrolysis constants derived in perchlorate solutions with those obtained in different media the relative extent of complex formation in these media may be compared, or if, in the case of perchlorate, $K_c = 0$, the actual values of the complexity constants may be calculated.

The apparent hydrolysis constants determined in perchlorate solutions K_1^P and K_2^P and those determined in solutions of X^- of the same ionic strength, K_1^X and K_2^X, are related to the true hydrolysis constants K_1 and K_2 by the expressions

$$K_1^P = \frac{K_1}{(1 + K_c[ClO_4]_T)}\ ; \qquad K_1^X = \frac{K_1}{(1 + K_X[X]_T)}$$

and

$$K_2^P = \frac{K_2}{(1 + K_c[ClO_4]_T)^2}\ ; \qquad K_2^X = \frac{K_2}{(1 + K_X[X]_T)^2}$$

from which it follows that

$$K_X = \frac{1}{[X]_T}\left\{\left(\frac{K_1^P}{K_1^X} - 1\right) + K_c[ClO_4]_T\,\frac{K_1^P}{K_1^X}\right\} \quad . \quad . \quad . \quad . \quad . \quad (8)$$

and also that

$$K_X = \frac{1}{[X]_T}\left\{\left(\sqrt{\frac{K_2^P}{K_2^X}} - 1\right) + K_c[ClO_4]_T\sqrt{\frac{K_2^P}{K_2^X}}\right\} \quad . \quad . \quad . \quad . \quad . \quad (9)$$

If K_c is assumed to be zero, then K_X, the formation constant for the ion UO_2X^+, may be readily calculated from the measured hydrolysis constants in the two media. Eqns. (8) and (9) may be used to detect complex formation by perchlorate ions. If it is known that K_X is not zero, and if K_1^P/K_1^X and K_2^P/K_2^X are <1, then $K_c > 0$, *i.e.*, formation of perchlorate complexes occurs. Implicit in this argument is the assumption that K_1 and K_2 (as defined above) remain unchanged when the medium is changed from one of perchlorate to one of X^-, *i.e.*, that all activity coefficients remain unchanged. This condition is unlikely to be fulfilled, as is shown, for example, by Robinson and Lim's work [14] on the activity coefficients of uranyl nitrate, chloride, and perchlorate; it is therefore preferable to rewrite eqns. (8) and (9) so as to include all the appropriate activity coefficient terms; they then become:

$$K_X = \frac{1}{\Pi_X^X[X]_T}\left\{\left(\frac{K_1^P\Pi_1^X}{K_1^X\Pi_1^P} - 1\right) + K_c\Pi_c^P[ClO_4]_T\,\frac{K_1^P\Pi_1^X}{K_1^X\Pi_1^P}\right\} \quad . \quad . \quad (8a)$$

and

$$K_X = \frac{1}{\Pi_X^X[X]_T}\left\{\left(\sqrt{\frac{K_2^P\Pi_2^X}{K_2^X\Pi_2^P}} - 1\right) + K_c\Pi_c^P[ClO_4]_T\sqrt{\frac{K_2^P\Pi_2^X}{K_2^X\Pi_1^P}}\right\} \quad . \quad (9a)$$

where the Π symbols represent the appropriate activity coefficient terms, the subscript denoting the constant concerned and the superscipt the nature of the medium. Note that

[14] Robinson and Lim, *J.*, 1951, 1840.

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Π_1^X and Π_1^P apply to K_1 in the two media and not to the experimental quantities K_1^X and K_1^P; similarly Π_2^X and Π_2^P apply to K_2. Unfortunately data at present available are insufficient to provide a valid test of these relations.

The quantities K_1 and K_2 given in Table 4 (in the nomenclature of the last section these would be K_1^P and K_2^P) may be used to calculate the heat content, free energy, and entropy changes associated with reactions (1) and (3). The values obtained are given in Table 5.

TABLE 5.

Temp. = 25·0°. μ = 0·0347.

	ΔH (kcal./mole)	ΔF (kcal./mole)	ΔS (cal./°c)
K_1	20·8	8·0	43
K_2	6·7	8·4	−6

The large value of ΔH for reaction (2) compared with reaction (1) makes it easy to see why evidence for its occurrence is not readily obtained at room temperature and leads to the conclusion that it would become the dominant process at sufficiently high temperatures. This possibility was, in fact, predicted by Kraus [1] who also calculated a value of ΔS for reaction (3) of 16 cal./°c. Detailed calculations based on the values in Table 5 would be of little value owing to the obvious crudity of the measurements of K_1 and K_2.

We are greatly indebted to Dr. J. Faucherre of the Université de Paris for much valuable correspondence and in particular for his kindness in making available to us a copy of his doctoral thesis and for access to his original experimental results.

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416. *Aromatic Substitution. Part III.* Alkylation of Aromatic Compounds by the Boron Trifluoride-catalysed Reaction of Alkyl Fluorides.*

By G. OLÁH, S. KUHN, and J. OLÁH.

The alkylation of aromatic compounds by boron trifluoride-catalysed reaction with alkyl fluorides has been examined. Alkyl fluoride–boron trifluoride complexes have been isolated.

WOHL and WERTYPOROCH [1] attempted to alkylate benzene with alkyl chlorides in the presence of boron trifluoride as catalyst. Burwell and Archer [2] failed to alkylate toluene similarly with *cyclo*hexyl bromide or chloride, but showed that benzene is readily alkylated by *cyclo*hexyl fluoride in the presence of boron trifluoride. They assumed that the BF_4^- anion, formed in this case by co-ordination with BF_3, is much more stable than the BF_3Cl^- or the BF_3Br^- anion. Hennion and Kurz [3] observed that, in the presence of water or alcohol, benzene or toluene could be alkylated by means of alkyl chlorides or bromides and boron trifluoride; they assumed that the reaction is assisted by the water–boron trifluoride and alcohol–boron trifluoride complexes.

In our studies, we examined the alkylation of aromatic compounds, chiefly alkylbenzenes, by boron trifluoride-catalysed reaction with alkyl fluorides.

The alkyl fluorides required were prepared partly by halogen exchange of silver fluoride with alkyl iodides [4] and partly by our modification [5] of the method by Nakanishi, Myers, and Jensen [6] for the decarboxylation of fluoroformic esters.

* Part II, *J.*, 1956, 4257.

[1] Wohl and Wertyporoch, *Ber.*, 1931, **64**, 1360.
[2] Burwell and Archer, *J. Amer. Chem. Soc.*, 1942, **64**, 1032.
[3] Hennion and Kurz, *ibid.*, 1943, **65**, 1001.
[4] Moisson, *Compt. rend.*, 1888, **107**, 99, 260.
[5] Oláh and Kuhn, *J. Org. Chem.*, in the press.
[6] Nakanishi, Myers, and Jensen, *J. Amer. Chem. Soc.*, 1955, **77**, 3099, 5033.

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We found that methyl, ethyl, propyl, *iso*propyl, *tert.*-butyl, or *cyclo*hexyl fluoride in the presence of boron trifluoride alkylates aromatic compounds in good yields, usually without resin formation. Yields (%) are shown in the Table.

RF	PhMe	*m*-$C_6H_4Me_2$	*s*-$C_6H_3Me_3$	RF	PhMe	C_6H_6
MeF	62	—	—	Pr^iF	84	—
EtF	81	83	79	Bu^tF	68	—
Pr^nF	77	—	—	$C_6H_{11}F$	79	85

The Lewis-acid complexes formed by the alkyl halides and catalysts have been examined by numerous authors. According to the generally accepted older ideas about the mechanism of the Friedel–Crafts alkylation, the alkyl halides are directly ionised by the Lewis-acid catalysts:[7] $RX + MX_3 \rightleftharpoons R^+MX_4^-$. The pure carbonium-ionic mechanism is supported primarily by the conductivity of solutions of aluminium chloride, aluminium bromide, and ferric chloride in various alkyl halides,[8,9] and by isotopic studies.[10]

H. C. Brown and his co-workers, on the basis of their experiments on the gallium chloride, aluminium chloride, aluminium bromide, and aluminium iodide complexes of methyl and ethyl halides, concluded that in these cases only a polar alkyl halide–metal halide complex is formed. However, they assume the formation of a different carbonium-ion complex for tertiary alkyl halides, which are easily ionised.[11] The existence of the ionic Lewis-acid complexes of alkyl halides was similarly shown by studies which proved primarily the isomerisation of alkyl halides under the influence of aluminium halides.[12]

Schneider and his co-workers [13] examined the isomerisation of *iso*alkyl compounds in the presence of alkyl fluoride and boron trifluoride, first with *iso*propyl and *tert.*-butyl fluoride; although (according to Ipatieff and Grosse [14]) the *iso*alkanes do not react with boron trifluoride and no isomerisation occurs, adding a little alkyl fluoride in the *iso*alkane causes boron trifluoride to dissolve in amount equivalent to the alkyl fluoride and isomerisation then takes place. Schneider *et al.*[13] did not examine these intermediate complexes, and no complex between alkyl halide and Lewis-acid type catalyst was obtained isolated pure.

By analogy with our earlier work on nitronium [15] and acylfluoroborates,[16] we attempted to isolate the alkyl fluoride–boron trifluoride complexes at low temperatures. Between −50°

R in $R^+BF_4^-$	M. p.	κ (10^{-2} ohm^{-1} cm.$^{-1}$)	Colour	R in $R^+BF_4^-$	M. p.	κ (10^{-2} ohm^{-1} cm.$^{-1}$)	Colour
Me	−110°	0·0002	None	Pr^i	−95°	0·4	Yellow
Et	−105	0·0005	,,	Bu^t	−80	0·4	,,
Pr^n	− 95	0·4	Yellow	C_6H_{11} ...	−54 to −52	0·5	,,

and −110° saturating the alkyl fluorides with boron trifluoride gave a 1 : 1 molar complex (calculated from the amount of boron trifluoride absorbed). The Table contains the melting points or decomposition points of the complexes isolated, and their specific

[7] Hammett, "Physical Organic Chemistry," New York, McGraw-Hill Book Co., 1940; Price, "Organic Reactions," Vol. III, New York, John Wiley and Sons, 1946.
[8] Wohl and Wertyporoch, *Ber.*, 1931, **64**, 1357; Wertyporoch, *ibid.*, p. 1369; Wertyporoch and Firla, *Z. phys. Chem.*, 1932, **162**, *A*, 398; Wertyporoch, Kowalski, and Roeske, *Ber.*, 1933, **66**, 1232; Wertyporoch and Kowalski, *Z. phys. Chem.*, 1933, **166**, *A*, 205.
[9] Fairbrother, *Trans. Faraday Soc.*, 1941, **37**, 763.
[10] *Idem*, *J.*, 1937, 503.
[11] Brown, Pearsall, Eddy, Wallace, Grayson, and Nelson, *Ind. Eng. Chem.*, 1953, **45**, 1462.
[12] Kekulé and Schrotter, *Ber.*, 1879, **12**, 2279; Gustavson, *J. prakt. Chem.*, 1886, **34**, 161; *Ber.*, 1883, **16**, 958; Wibaut and Brouwer, *Rec. Trav. chim.*, 1934, **53**, 1001; Mayo and Dolmick, *J. Amer. Chem. Soc.*, 1944, **66**, 985; Nash, Taylor, and Doering, *ibid.*, 1949, **71**, 1516; Roberts, Ropp, and Neville, *ibid.*, 1955, **77**, 1764; Sixma and Hendriks, *Rec. Trav. chim.* 1956, **75**, 169.
[13] Schneider and Kennedy, *ibid.*, 1951, **73**, 5013, 5017, 5024; Donnell and Kennedy, *ibid.*, 1952, **74**, 4162.
[14] Ipatieff and Grosse, *ibid.*, 1935, **57**, 1617.
[15] Oláh and Kuhn, *Chem and Ind.*, 1956, 98; Oláh, Kuhn, and Mlinko, *J.*, 1956, 4257.
[16] Oláh and Kuhn, *Chem. Ber.*, 1956, **89**, 866.

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conductivities in the molten state. The specific conductivities of methyl and ethyl fluoroborate are less by three powers of ten than that of the propyl and butyl compounds. Thus the former have an only slightly dissociated polar covalent bond, while the propyl and *tert.*-butyl complexes have a much more dissociated ionic character owing to the greater possibility of stabilisation. (The boron trifluoride-assisted isomerisation of propyl and butyl fluoride will be discussed in another paper.)

The complexes isolated, when allowed to react at low temperatures with alkylbenzenes, gave the corresponding alkylated derivatives directly, in good yields.

Our experiments gave a direct experimental proof of the H. C. Brown's results [11] in a different field. According to these, the intermediate complexes formed with catalysts of Lewis-acid type during alkylations with alkyl halides fall into two classes: 1 : 1 addition complexes, containing a polarised covalent bond (in our experiments the methyl and ethyl complexes); and the considerably ionised complexes of ionic character (in our experiments, the propyl and *tert.*-butyl complexes).

Experimental

Alkylations with Alkyl Fluorides in the Presence of Boron Trifluoride.—Alkyl fluoride (0·5 mol.) was dissolved in alkylbenzene (1 mol.) at −20° to −80°. Boron trifluoride was passed into the solution till it became saturated (0·5 mol. absorbed), during which a coloured lower phase separated. The mixture was allowed to warm to above the decomposition point of the complex; there was copious evolution of boron trifluoride. The organic layer was separated, washed free from acid, dried, and fractionated. After removal of the excess of the original alkylbenzene, the fraction containing the monoalkylated isomers was separated without trying to separate the isomers by distillation. In the alkylation of benzene with *cyclo*hexyl fluoride the solution was saturated with boron trifluoride with ice-cooling.

Separation of the Boron Trifluoride Complexes of Alkyl Fluorides.—Boron trifluoride was passed into alkyl fluoride (0·5 mol.) at −50° to −110°. 0·5 mol. was absorbed, giving a colourless product with methyl and ethyl fluoride, and a coloured product with propyl, *tert.*-butyl, and *cyclo*hexyl fluoride. The complexes were frozen with liquid air and were then allowed to warm slowly, in order to determine their m. p.s or decomp. points.

The preparations were carried out in silica apparatus under anhydrous conditions.

The molar composition of the complexes was proved in part by measuring the amount of boron trifluoride taken up, and in part by determination of the BF_4^- content as nitron fluoroborate.

Determination of Conductivity.—This was generally done with 30 ml. of material (molten), in a silica vessel; an immersed silica conductivity vessel with platinised platinum electrodes (conductivity constant 0·71; 0·1N-HCl), a Wheatstone-bridge apparatus, and an audiofrequency generator with a variable voltage and frequency as sources were used; measurements were carried out at 2 v with a frequency of 1000—2000. To make maximum sharpness, a condenser whose capacity could be varied between 1 pF and 10,000 pF, was connected in parallel to the resistance. The zero-instrument was a CRO, connected through an amplifier. The error of the determination was 0·5%.

Reaction of the Alkyl Fluoroborate with Toluene.—To the previously prepared ethyl, propyl, and *tert.*-butyl fluoroborate, an equimolar amount of toluene, cooled to −80°, was added, with vigorous stirring. The mixture became homogeneous, and on warming above the decomposition point of the complexes evolved boron trifluoride. After separation of the organic layer and washing of it acid-free, the monoalkylated products were isolated in 80—85% yield, with a little dialkylated product.

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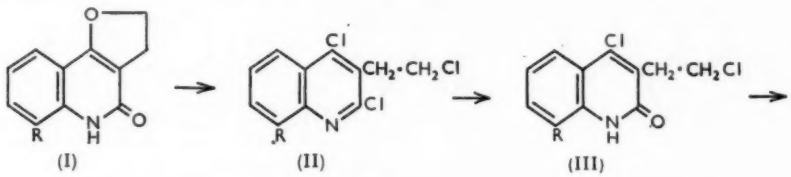
417. *The Synthesis of Dictamnine and γ-Fagarine.*

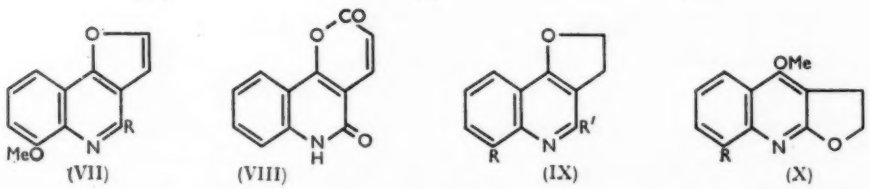
By M. F. Grundon and N. J. McCorkindale.

The alkaloids dictamnine (VI; R = H) and γ-fagarine (VI; R = OMe) have been synthesised from the angular dihydrofuranoquinolones (I; R = H, OMe). The structures of the intermediates have been confirmed by ultraviolet and infrared spectroscopy and by conversion into authentic furano-(2′ : 3′-2 : 3)quinoline.

The furanoquinoline alkaloids are generally regarded as derivatives of furano(2′ : 3′-2 : 3)quinoline. Only in dictamnine (VI; R = H) has the presence of this system been established unequivocally,[1,2,3,4] but there is strong evidence[3,4,5] for an analogous constitution for skimmianine (XVI; R = OMe). Other alkaloids have been studied less intensively: thus, the degradation[6] of γ-fagarine to 2 : 4-dihydroxy-8-methoxyquinoline does not distinguish between the structures (VI; R = OMe) and (VII; R = OMe) for the alkaloid.

The linear structures for dictamnine and γ-fagarine have now been established by a synthesis[7] indicated in the reaction scheme (I—VI).*





We have shown[2] that reaction of aniline or *o*-anisidine with ethyl (2-ethoxyethyl)-malonate gives exclusively the angular dihydrofuranoquinolones (I; R = H and OMe), probably *via* 2 : 4-dihydroxyquinolines. Ring closure involving a 4-hydroxy-group is

* *Added, March 15th*, 1957.—A synthesis of dictamnine was reported briefly by Sato and Ohta (*J. Chem. Soc. Japan*, 1956, **77**, 1630). We thank Dr. T. Sato for informing us of this work. Unpublished syntheses of furano(2′ : 3′-2 : 3)quinoline by King, Latham, and Partridge, and of dihydrodictamnine by Cook and Haynes are mentioned by Price (*Fortschr. Chem. org. Naturstoffe*, 1956, **13**, 320).

[1] Asahina, Ohta, and Inubuse, *Ber.*, 1930, **63**, 2045.
[2] Grundon, McCorkindale, and (in part) Rodger, *J.*, 1955, 4284.
[3] Brown, Hobbs, Hughes, and Ritchie, *Austral. J. Chem.*, 1954, **7**, 348.
[4] Ohta and Mori, *Ann. Reports Tokyo Coll. Pharm.*, 1955, **5**, 48.
[5] Asahina and Inubuse, *Ber.*, 1930, **63**, 2052.
[6] Berinzaghi, Maruzabal, Labriola, and Deulofeu, *J. Org. Chem.*, 1945, **10**, 181.
[7] Cf. Grundon and McCorkindale, *Chem. and Ind.*, 1956, 1091.

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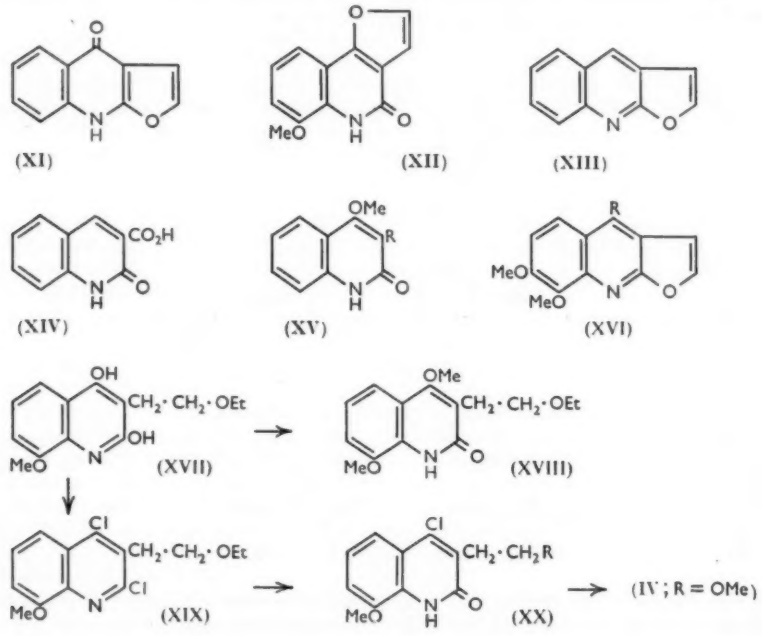
also involved in the formation [8] of the pyronoquinolone (VIII) from 2 : 4-dihydroxyquinoline and malic acid, and in the synthesis of flindersine.[8] Thus, linear furanoquinolines are unlikely to result directly from dihydroxyquinoline derivatives. We expected that 4-chloro-2-quinolones would be more useful intermediates.

The dihydrofuranoquinolone (I; R = H) with phosphorus oxychloride gave 2 : 4-dichloro-3-2′-chloroethylquinoline (II; R = H),[2] now obtained in higher yield (59%) by modifying the reaction conditions. A by-product, $C_{11}H_8ONCl$, was isolated with properties expected for the angular dihydrofuranoquinoline (IX; R = H, R′ = Cl). The trichloro-compound (II; R = H) is conveniently prepared from aniline and ethyl (2-ethoxyethyl)malonate without purification of the intermediate dihydrofuranoquinolone. Treatment of the dihydrofuranoquinolone (I; R = OMe) with phosphorus oxychloride afforded the trichloro-derivative (II; R = OMe) and the chlorodihydrofuranoquinoline (IX; R = OMe, R′ = Cl).

The successful preparation [9] of 4 : 7-dichloro-1 : 2-dihydro-2-oxoquinoline by acid hydrolysis of 2 : 4 : 7-trichloroquinoline led us to examine this reaction as a general method for preparing 4-chloro-2-hydroxyquinolines. 2 : 4-Dichloro-3-ethoxycarbonylquinoline was hydrolysed to 4-chloro-3-ethoxycarbonyl-1 : 2-dihydro-2-oxoquinoline (by M. N.

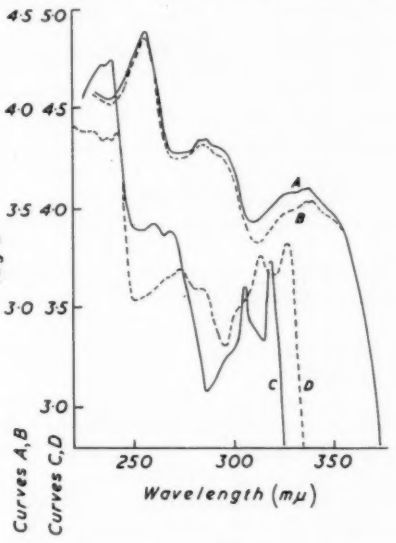


Rodger), and by the same method the two trichloro-compounds (II; R = H) and (II; R = OMe) furnished, in good yield, the dichloro-derivatives (III; R = H) and (III; R = OMe). The three products had the properties of 2-quinolones, namely, insolubility in dilute aqueous alkali, infrared maxima at 1654—1650 cm.$^{-1}$ (NH·CO in a 2-quinolone), and intense ultraviolet absorption at 2720—2870 Å.

Chromatography of the chloroquinolone (III; R = H) on alkaline alumina afforded the linear dihydrofuranoquinoline (IV; R = H) (40%), and this ring closure was effected

[8] Brown, Hughes, and Ritchie, *Austral. J. Chem.*, 1956, **9**, 279.
[9] Rowlett and Lutz, *J. Amer. Chem. Soc.*, 1946, **68**, 1290.

almost quantitatively with silver oxide in aqueous ethanol. 4-Chloro-4′ : 5′-dihydro-8-methoxyfurano(2′ : 3′-2 : 3)quinoline (IV; R = OMe) was prepared in the same way from the corresponding dichloro-compound (III; R = OMe). Reaction with sodium methoxide furnished the methoxydihydrofuranoquinolines (X; R = H and OMe). The properties of the former compound correspond to those recorded [10] for dihydrodictamnine, prepared by reduction of the alkaloid. Dehydrogenation of the chlorodihydrofuranoquinoline (IV; R = OMe) with palladium–charcoal gave the chlorofuranoquinoline (V; R = OMe) in small amount, whereas reaction with *N*-bromosuccinimide and treatment of the crude intermediate with diethylaniline gave a high yield of this compound. The products from these reactions had identical infrared spectra, but that obtained by the bromination-dehydrobromination technique did not give satisfactory analyses, possibly because of the presence of an impurity containing aromatic bromine. Application of the same reaction to 4-chloro-4′ : 5′-dihydrofurano(2′ : 3′-2 : 3)quinoline (IV; R = H) gave the corresponding furanoquinoline (V; R = H) and similar difficulties were encountered in the purification of the product. Reaction with sodium methoxide afforded the methoxyfuranoquinoline



Ultraviolet-light absorption in ethanol of the by-product from the reaction of 4-*chloro*-8-*methoxyfurano*(2′ : 3′-2 : 3)*quinoline with sodium methoxide* (*A*), 4-*chloro*-3-2′-*ethoxyethyl*-1 : 2-*dihydro*-8-*methoxy*-2-*oxoquinoline* (*B*), 2-*methoxyfurano*(3′ : 2′-3 : 4)*quinoline* (*C*), *and* 4-*chloro*-4′ : 5′-*dihydrofurano* (2′ : 3′-2 : 3)*quinoline* (*D*).

(VI; R = H), identical with dictamnine. The chlorofuranoquinoline (V; R = H) was hydrolysed by acid to the 4-quinolone (XI), identical with a sample of nordictamnine obtained from the alkaloid. The chlorofuranoquinoline (V; R = OMe) was converted by sodium methoxide into the methoxy-derivative (VI; R = OMe), indistinguishable from γ-fagarine. Analyses for a by-product of this reaction agreed best with the formula $C_{11}H_8ONCl(OMe)_2,\frac{1}{2}H_2O$. As the ultraviolet spectrum is almost identical with that of the 2-quinolone (XX; R = OEt) (see Figure), we suggest provisionally that the compound is the chloroquinolone (XX; R = OMe). The infrared absorption at 1631 cm.$^{-1}$ is slightly lower than that shown by most 2-quinolones, but the band has the shape and very high intensity characteristic of 2-quinolone absorption. The by-product may arise by attack of OMe^- on the furan ring, with subsequent reduction.

Infrared and ultraviolet spectra are valuable for distinguishing 2- from 4-quinolones.[11] Our results (Table 1) support the generalisation that 2-quinolones show ultraviolet absorption at 2700—2850 Å (ε 6300—9000) absent in 4-quinolones, and that the long-wavelength

[10] Cook and Haynes, *Austral. J. Chem.*, 1954, **7**, 273.
[11] For discussion and refs. see ref. 2 and Mason, *Chem. Soc. Special Publ. No.* 3, 1955, p. 139.

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band is more intense in 4-quinolones. Further, strong amide-carbonyl infrared absorption occurs at 1660—1640 cm.$^{-1}$ in 2-quinolones whereas 4-quinolones show weaker maxima at lower frequencies (1620—1630 cm.$^{-1}$). It appears that 2-methoxyquinolines or dihydrofurano(2′ : 3′-2 : 3)quinolines show in their spectra (Nos. 1—7 of Table 2, and Figure) some of the characteristics of 2-quinolones. Furano(2′ : 3′-2 : 3)quinolines show normal behaviour (see, for example, Nos. 8—11 of Table 2).

The structures of the intermediates (IV—VI, and X) are also supported by non-identity with the angular isomers of established structure.[2] In order to complete the series, the furanoquinolone (XII) [2] was converted through the chloro-derivative (VII; R = Cl) into 2 : 8-dimethoxyfurano(3′ : 2′-3 : 4)quinoline (VIII; R = OMe), an isomer of γ-fagarine.

TABLE 1. *Infrared absorption bands* (KBr *disc*) *and ultraviolet absorption* (*in ethanol*) *of 2- and 4-quinolones.*

		Main ultraviolet absorption maxima					
No.	Substance	λ	ε	λ	ε	λ	ε
1	3-Carboxy-2-quinolone	228	42,700	289	10,000	348	5,500
2	(III; R = H)	228	35,500	272	8,100	330	7,400
3	(III; R = OMe)	257	27,500	287	7,200	340	3,500
4	4-Chloro-3-ethoxycarbonyl-2-quinolone	228	28,200	275	7,700	335	6,200
5	(XX; R = OEt)	256	21,900	285	6,500	338	3,400
6	(XVIII)	252	22,900	278	6,900	326	3,300
7	3-Carboxy-4-quinolone	245	18,600	—	—	308	12,300
8	(XI)	245	44,700	—	—	329	14,800
	Nor-γ-fagarine [12]	242	47,900	—	—	329	11,300
	iso-γ-Fagarine [12]	246	43,400	—	—	336	12,200
	Norskimmianine [12]	253	40,600	—	—	326	9,400
	*iso*Skimmianine [12]	258	45,800	—	—	331	11,400
	*iso*Kokusaginine [13]	252	50,300	—	—	327 342	10,000 10,000

	Infrared maxima (cm.$^{-1}$).				
No.	2-Quinolone amide I	No.	2-Quinolone amide I	No.	4-Quinolone amide I
1	1651	4	1648	7	1620
2	1650	5	1641	8	1625
3	1650	6	1644		

TABLE 2. *Infrared absorption* (KBr *disc*) *in the region* 1700—1630 *cm.*$^{-1}$ *and ultraviolet absorption* (*in ethanol*) *of quinolines with an ether function in the 2-position.*

			Main ultraviolet absorption maxima					
No.	Substance	Infrared *	λ	ε	λ	ε	λ	ε
1	(X; R = H)	1631	228	46,800	270	7,600	317	4,900
2	(X; R = OMe)	1635	247	38,900	278	6,600	322	2,500
3	(IV; R = H)	1645	242	24,000	274	4,900	327	6,600
4	(IV; R = OMe)	1642	254	38,900	289	4,000	325	3,300
5	(IX; R = H, R′ = OMe)	1641	230	38,000	276	5,400	314	1,900
6	2-Methoxyfurano(3′ : 2′-3 : 4)-quinoline	1637	239	56,200	261	8,300	317	5,400
7	(VII; R = OMe)	1642	246	49,000	—	—	308	1,200
8	(VI; R = H)	—	235	58,900	—	—	312	8,700
9	(VI; R = OMe)	—	242	60,300	—	—	308	6,600
10	(V; R = H)	—	240	64,500	—	—	312	1,230
11	(V; R = OMe)	—	250	47,900	—	—	322	8,100
12	(XIII)	—	234	50,300	—	—	306	1,100

* All the infrared peaks are of medium intensity.

The angular chlorodihydrofuranoquinoline (IX; R = H, R′ = Cl) with sodium methoxide furnished the corresponding methoxy-compound (IX; R = H, R′ = OMe), an isomer of dihydrodictamnine.

The chlorofuranoquinoline (V; R = H) with hydrazine hydrate gave the hydrazino-derivative which, without purification, was converted by aqueous copper sulphate into furano(2′ : 3′-2 : 3)quinoline (XIII). Permanganate oxidation of this compound to

3-carboxy-2-quinolone (XIV) demonstrates conclusively the linear structure of the precursors.

Our experience with synthetic furanoquinolines suggests alternative methods of determining the structure of furanoquinoline alkaloids. A study of the properties of the nor- and *iso*-derivatives provides the best preliminary indication of the structures of the alkaloids. For example, the 4-quinolone nature of nor-γ-fagarine is clearly suggested by its ultraviolet spectrum,[12] and by its solubility in aqueous alkali.[12] Published data [12, 13] (Table 1) indicate analogous constitutions for the requisite derivatives of skimmianine and kokusaginine. The established methods of degradation require oxidation [1, 5, 6] to a quinoline acid (XV; R = CO_2H, for dictamnine) or hydrogenation [14] to a 3-ethylquinoline (XV; R = Et, for dictamnine). These have been synthesised from the corresponding 2 : 4-dihydroxyquinolines and diazomethane,[2, 3, 4] but the selective methylation of the 4-hydroxy-group is based only on analogy with 2 : 4-dihydroxyquinoline. Further, this reaction is not applicable [15] to all 2 : 4-dihydroxyquinolines, and additional evidence is desirable to complete the proof of structure. In the case of dictamnine this was provided [2] by conversion of ethyl dictamnate (XV; R = CO_2Et) to 3-carboxy-2-chloro-4-methoxyquinoline of established constitution. A more satisfactory procedure might involve oxidation of the unsubstituted furanoquinolines prepared from the chlorofuranoquinolines by the method described above and used previously for the angular isomers. The chlorofuranoquinolines are likely to be readily available from the hydrolysis products of the alkaloids and, indeed, we have shown that nordictamnine with phosphorus oxychloride gives an excellent yield of the chlorofuranoquinoline (V; R = H). The alkaloid skimmianine (XVI; R = OMe) is converted [16] directly into the hydrazino-derivative (XVI; R = $NH{\cdot}NH_2$) and use of this process would shorten the proposed reaction sequence.

Our earlier attempts [2] to synthesise γ-fagarine employed 3-2′-ethoxyethyl-2 : 4-dihydroxy-8-methoxyquinoline (XVII). An improved preparation is described in the Experimental section. Reaction with diazomethane gave 3-2′-ethoxyethyl-1 : 2-dihydro-4 : 8-dimethoxy-2-oxoquinoline (XVIII), a constitution confirmed by its infrared and ultraviolet spectra (Table 1).

Ring closure to a linear furanoquinoline did not occur, the quinolone being recovered after prolonged heating in diphenyl ether or with polyphosphoric acid. The dihydroxyquinoline (XVII) was converted quantitatively into the corresponding dichloro-compound (XIX), hydrolysed by hydrochloric acid to a monochloro-quinoline having the characteristic properties (Table 1) of a 2-quinolone of structure (XX; R = OEt). This compound in boiling diphenyl ether afforded the chlorodihydrofuranoquinoline (IV; R = OMe). This constitutes an alternative synthesis of γ-fagarine, but the yield of the chlorodihydrofuranoquinoline, based on *o*-anisidine, compares unfavourably with that obtained in the previous preparation.

Experimental

2 : 4-*Dichloro*-3-2′-*chloroethylquinoline* (II; R = H).—(*a*) **1 : 2 : 4′ : 5′-Tetrahydro-2-oxofurano(3′ : 2′-3 : 4)quinoline** (7·91 g.) and phosphorus oxychloride (50 c.c.) were heated under reflux for 3½ hr., the phosphorus oxychloride was removed and water added. The precipitate (9·4 g.), dissolved in 1 : 1 benzene–light petroleum (b. p. 60—80°), was chromatographed on alumina. Elution with the same solvent gave 2 : 4-dichloro-3-2′-chloroethylquinoline (6·74 g., 59%), m. p. 99—100°, crystallising from ethanol in colourless needles, m. p. 110—112°. Further elution with the same solvent gave *2-chloro-4′ : 5′-dihydrofurano*(3′ : 2′-3 : 4)*quinoline* (0·73 g., 8%), separating from ethanol in colourless prisms, m. p. 162—163° (Found : C, 64·2; H, 4·2; N, 7·3; Cl, 17·8. $C_{11}H_8ONCl$ requires C, 64·2; H, 3·9; N, 6·8; Cl, 17·2%).

[12] Deulofeu and Bassi, *Anal. Asoc. quím. argentina*, 1952, **40**, 249.
[13] Lamberton and Price, *Austral. J. Sci. Res.*, 1953, **6**, 69.
[14] Ohta, *J. Pharm. Soc. Japan*, 1953, **73**, 63.
[15] Brown, *Austral. J. Chem.*, 1955, **8**, 121.
[16] Ohta, Miyazaki, and Mori, *Ann. Reports Tokyo Coll. Pharm.*, 1954, **4**, 7.

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(*b*) Crude 1 : 2 : 4′ : 5′-tetrahydro-2-oxofurano(3′ : 2′-3 : 4)quinoline [prepared from aniline (29·2 g.)] was refluxed with phosphorus oxychloride (400 c.c.) for 3½ hr., the excess of phosphorus oxychloride was removed, and the residue shaken with chloroform and water. The chloroform layer was separated, dried, and evaporated, and the residue was extracted with boiling light petroleum (b. p. 40—60°) (300 c.c.). Concentration of the light petroleum solution afforded the trichloro-compound as colourless needles (16·87 g.), which began to soften at 100° and melted at 108—111°, suitable for subsequent reaction. The petroleum-insoluble material, dissolved in benzene, was chromatographed on alumina. Elution with benzene gave a further quantity of the trichloro-compound (9·77 g.; total yield 26·3 g., 32% based on aniline). Further elution of the column gave a white solid, m. p. 152—156° alone or mixed with 2-chloro-4′ : 5′-dihydrofurano(3′ : 2′-3 : 4)quinoline obtained as in (*a*).

2 : 4-*Dichloro*-3-2′-*chloroethyl*-8-*methoxyquinoline* (II; R = OMe).—1 : 2 : 4′ : 5′-Tetrahydro-8-methoxy-2-oxofurano(3′ : 2′-3 : 4)quinoline (7·38 g.) and phosphorus oxychloride were refluxed for 3½ hr., the excess of reagent was removed, and the residue treated with water to give a brown solid (7·5 g.), m. p. 90—92°, which was extracted (Soxhlet) with light petroleum (b. p. 40—60°), leaving a residue (A). On concentration of the extract, the *trichloro*-derivative separated as a pale yellow solid (5·72 g., 58%), m. p. 107—109°. It crystallised from light petroleum (b. p. 40—60°) in colourless needles, m. p. 108—109° (Found: C, 49·9; H, 3·6; N, 4·9; Cl, 35·9. $C_{12}H_{10}ONCl_3$ requires C, 49·6; H, 3·5; N, 4·8; Cl, 36·6%).

The residue (A) (0·82 g., 10%), m. p. 145—158°, consisted of 2-*chloro*-4′ : 5′-*dihydro*-8-*methoxyfurano*(3′ : 2′-3 : 4)*quinoline* and crystallised from ethanol in colourless needles, m. p. 162° (Found: C, 59·1; H, 4·5; Cl, 15·0. $C_{12}H_{10}O_2NCl,\frac{1}{2}H_2O$ requires C, 58·9; H, 4·5; Cl, 14·5%).

4-*Chloro*-3-*ethoxycarbonyl*-1 : 2-*dihydro*-2-*oxoquinoline* (with M. N. Rodger).—2 : 4-Dichloro-3-ethoxycarbonylquinoline (4·0 g.) was heated in 6N-hydrochloric acid (112 c.c.) and dioxan (100 c.c.) for 2 hr. Addition of water (1 l.) precipitated the *quinolone*, crystallising from ethyl acetate in needles (1·63 g., 44%), m. p. 202—203° (Found: C, 57·1; H, 3·8; N, 5·7. $C_{12}H_{10}O_3NCl$ requires C, 57·3; H, 4·0; N, 5·6%), insoluble in aqueous alkali, and giving no colour with ferric chloride.

4-*Chloro*-3-2′-*chloroethyl*-1 : 2-*dihydro*-2-*oxoquinoline* (III; R = H).—(*a*) 2 : 4-Dichloro-3-2′-chloroethylquinoline (1 g.), 6N-hydrochloric acid (28 c.c.), and dioxan (22 c.c.) were refluxed for 3 hr. and kept at room temperature for 12 hr. The precipitate (0·45 g.), m. p. 169—175°, was extracted with boiling aqueous methanol, and the insoluble residue (0·04 g.) removed. The *quinolone* separated from the solution in needles (0·26 g., 29%), m. p. 169—175° raised to 174—175° by crystallisation from methanol (Found: C, 54·7; H, 3·8; Cl, 29·0. $C_{11}H_9ONCl_2$ requires C, 54·6; H, 3·7; Cl, 29·3%). The compound, when heated above its m. p., resolidified in needles, m. p. >300°. It was insoluble in aqueous alkali, and gave only a faint yellow colour with ferric chloride in ethanol.

(*b*) The trichloro-compound was hydrolysed as described above except that heating was discontinued after 1 hr. 10 min. After 12 hr. at room temperature the quinolone was obtained as needles (0·43 g., 47%), m. p. and mixed m. p. 171—177°. Dilution of the acid solution with an equal volume of water precipitated 2 : 4-dichloro-3-2′-chloroethylquinoline (0·15 g.), m. p. and mixed m. p. 109—111°.

4-*Chloro*-3-2′-*chloroethyl*-1 : 2-*dihydro*-8-*methoxy*-2-*oxoquinoline* (III; R = OMe).—Hydrolysis of 2 : 4-dichloro-3-2′-chloroethyl-8-methoxyquinoline (2·82 g.) with 6N-hydrochloric acid (79 c.c.) and dioxan (62 c.c.) as in (*a*) above gave the *chloroquinolone* in colourless needles (1·6 g., 57%), m. p. 190—193°, unchanged by crystallisation from methanol (Found: C, 53·1; H, 4·0; N, 5·3; Cl, 26·0. $C_{12}H_{11}O_3NCl_2$ requires C, 53·0; H, 4·1; N, 5·1; Cl, 26·1%), insoluble in dilute aqueous alkali, and giving no colour with ferric chloride.

4-*Chloro*-4′ : 5′-*dihydrofurano*(2′ : 3′-2 : 3)*quinoline* (IV; R = H).—(*a*) 4-Chloro-3-2′-chloroethyl-1 : 2-dihydro-2-oxoquinoline (1·94 g.) in ethanol (130 c.c.) and water (90 c.c.) was refluxed for 3 hr. with silver oxide (from silver nitrate, 6 g.). The filtered solution was concentrated to remove ethanol and extracted with chloroform. Evaporation of the chloroform gave the *dihydrofuranoquinoline* (1·59 g., 97%), m. p. 105—111°, suitable for subsequent reactions. Purification by chromatography on alumina, elution with benzene, evaporation, and crystallisation from aqueous ethanol gave rods, m. p. 115—116° (Found: C, 64·6; H, 4·0. $C_{11}H_8ONCl$ requires C, 64·2; H, 3·8%).

(*b*) A solution of the chloroquinolone (0·19 g.) in benzene was chromatographed over alumina.

Elution with benzene gave the dihydrofuranoquinoline (0·073 g., 45%), m. p. and mixed m. p. 110—112°.

4-Chloro-4′ : 5′-dihydro-8-methoxyfurano(2′ : 3′-2 : 3)quinoline (IV; R = OMe).—(a) *From 4-chloro-3-2′-chloroethyl-1 : 2-dihydro-8-methoxy-2-oxoquinoline.* As above (silver oxide), the chloroquinolone (0·5 g.) was converted into the *dihydrofuranoquinoline* (0·41 g., 95%), separating from ethanol in needles, m. p. 186—188° (Found: C, 61·7; H, 4·6; Cl, 14·5. $C_{12}H_{10}O_2NCl$ requires C, 61·2; H, 4·3; Cl, 15·0%).

(b) *From 4-chloro-3-2′-ethoxyethyl-1 : 2-dihydro-8-methoxy-2-oxoquinoline* (see below). A solution of the chloroquinolone (1 g.) in diphenyl ether (25 c.c.) was heated under reflux for 4 hr. Addition of light petroleum (b. p. 40—60°) yielded starting material (0·33 g.), m. p. and mixed m. p. 156—160°. The light petroleum–diphenyl ether solution was concentrated to small bulk, and the diphenyl ether removed by steam-distillation. The residue separated from ethanol in needles (0·28 g.), m. p. 146—149°, but repeated crystallisation from ethanol effected no further purification. The crude material in benzene was chromatographed on acid-washed alumina. Elution with benzene gave the furanoquinoline (0·16 g., 19%), m. p. and mixed m. p. 186—188°. Elution of the column with chloroform gave a further quantity (0·07 g.) of the chloroquinolone (total recovery, 0·40 g., 40%).

4′ : 5′-Dihydro-4-methoxyfurano(2′ : 3′-2 : 3)quinoline (X; R = H).—4-Chloro-4′ : 5′-dihydrofurano(2′ : 3′-2 : 3)quinoline (0·5 g.) in a methanol solution of sodium methoxide [from sodium (0·5 g.) and methanol (10 c.c.)] was heated under reflux for 4 hr. The methanol was removed, water added, the mixture extracted with chloroform, and the chloroform evaporated. The residue, in benzene, was chromatographed on alumina. Elution with benzene gave the *dihydromethoxyfuranoquinoline* (0·31 g., 63%), m. p. 102—105°. The analytical sample crystallised from light petroleum (b. p. 60—80°) in colourless needles, m. p. 104—105° (lit.,[10] m. p. 103—104°) (Found: C, 71·5; H, 5·5; N, 6·9; OMe, 14·9. $C_{12}H_{11}O_2N$ requires C, 71·6; H, 5·5; N, 7·0; 1OMe, 15·4%).

4′ : 5′-Dihydro-4 : 8-dimethoxyfurano(2′ : 3′-2 : 3)quinoline (X; R = OMe).—By the method described in the previous experiment 4-chloro-4′ : 5′-dihydro-8-methoxyfurano(2′ : 3′-2 : 3)-quinoline was converted into the crude *dimethoxydihydrofuranoquinoline*, crystallising from aqueous ethanol in needles (0·12 g., 61%), m. p. 163—168°. After chromatography in benzene on alumina, a sample had m. p. 168—170° (Found: C, 67·9; H, 6·1; N, 5·7. $C_{13}H_{13}O_3N$ requires C, 67·5; H, 5·7; N, 6·1%).

4-Chlorofurano(2′ : 3′-2 : 3)quinoline (V; R = H).—(a) *From 4-chloro-4′ : 5′-dihydrofurano-(2′ : 3′-2 : 3)quinoline.* The dihydrofuranoquinoline (3 g.), *N*-bromosuccinimide (3·2 g.), a trace of benzoyl peroxide, and carbon tetrachloride (100 c.c.) were heated under reflux for 2 hr. The mixture, at room temperature, was filtered and the solution was evaporated under reduced pressure. The residue was refluxed with diethylaniline (30 c.c.) for 3 hr., added to 3N-hydrochloric acid (250 c.c.), and extracted with ether. Evaporation of the ether yielded an orange solid (2·36 g.), m. p. 105—110°, which was chromatographed in benzene on alumina. Elution with benzene afforded the furanoquinoline (2·05 g., 59%), m. p. 105—113°, crystallising from methanol in colourless rods, m. p. 112—114° (Found: C, 62·4; H, 3·3; Cl, 17·1%). The analytical data were unsatisfactory, but the product was shown to be identical with an authentic sample prepared as in (b) below by a mixed m. p. determination and by infrared spectra.

(b) *From nordictamnine* (see below).—Nordictamnine (0·056 g.) and phosphorus oxychloride (1 c.c.) were heated under reflux for 1 hr. and the excess of reagent was removed under reduced pressure. Addition of water gave the *chlorofuranoquinoline* (0·051 g., 83%), m. p. 111—115°, separating from methanol (charcoal) in colourless needles, m. p. 114—116° (Found: C, 65·2; H, 3·0. $C_{11}H_6ONCl$ requires C, 64·9; H, 3·0%).

4-Chloro-8-methoxyfurano(2′ : 3′-2 : 3)quinoline (V; R = OMe).—(*a*) A solution of 4-chloro-4′ : 5′-dihydro-8-methoxyfurano(2′ : 3′-2 : 3)quinoline (1 g.) in diphenyl ether (10 c.c.) was refluxed for 13 hr. in the presence of 10% palladium–charcoal (0·75 g.). Light petroleum (b. p. 40—60°) was added to the cooled, filtered reaction mixture, the solution was decanted from a small quantity of yellow gum, and the light petroleum removed by evaporation and the diphenyl ether by steam-distillation. A yellow gum was obtained from the aqueous mixture with ether and chromatographed in benzene on alumina. Elution of the first yellow band with benzene gave the required *chlorofuranoquinoline* (0·05 g., 5%), m. p. 170—179°, separating from ethanol in pale yellow prisms, m. p. 178—180° (Found: C, 61·6; H, 3·6. $C_{12}H_8O_2NCl$ requires C, 61·7; H, 3·5%). Further elution with benzene gave unchanged dihydrofuranoquinoline (0·04 g.),

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m. p. and mixed m. p. 175—177°. Elution with benzene–chloroform (4 : 1) furnished 1 : 2 : 4′ : 5′-tetrahydro-8-methoxy-2-oxofurano(3′ : 2′-3 : 4)quinoline (0·009 g.), m. p. and mixed m. p. 202—206°.

(*b*) 4-Chloro-4′ : 5′-dihydro-8-methoxyfurano(2′ : 3′-2 : 3)quinoline (1 g.) was brominated-dehydrobrominated by the method applied above to 4-chloro-4′ : 5′-dihydrofurano(2′ : 3′-2 : 3)-quinoline. A solution of the crude product in benzene–light petroleum (20 : 1) was chromatographed on alumina. Elution with the same solvent gave the furanoquinoline (0·71 g., 72%), m. p. 163—171°, which crystallised from ethanol in colourless needles, m. p. 169—172° (mixed m. p. and infrared spectra).

Dictamnine (VI; R = H).—4-Chlorofurano(2′ : 3′-2 : 3)quinoline (0·11 g.) in methanolic sodium methoxide [from sodium (0·11 g.) and methanol (2·5 c.c.)] was refluxed for 3 hr. The methanol was evaporated, water added, and the mixture extracted with chloroform. Evaporation of the chloroform gave a yellow solid (0·11 g.) which was purified by chromatography on alumina. Elution with benzene gave *dictamnine* in colourless needles (0·036 g., 33%), m. p. 129—131°, raised by crystallisation from light petroleum (b. p. 60—80°) to 132° alone or mixed with an authentic sample (Found : C, 72·6; H, 4·6. $C_{12}H_9O_2N$ requires C, 72·4; H, 4·6%). The ultraviolet spectra [$\lambda_{max.}$ 308 (log ε 3·88), 312 (log ε 3·86), 328 mμ (log ε 3·82)] of the natural and the synthetic alkaloid were identical, and the infrared spectra were indistinguishable.

Nordictamnine (XI).—4-Chlorofurano(2′ : 3′-2 : 3)quinoline (1 g.) in 10N-hydrochloric acid (5 c.c.) and ethanol (20 c.c.) was heated under reflux for 10 hr., the ethanol removed, and the solution was made alkaline with 2N-aqueous sodium hydroxide and extracted with chloroform. The aqueous solution was acidified and the yellow precipitate (0·4 g.), m. p. 218—223°, sublimed at 190—195° (bath)/0·1 mm.

Nordictamnine was obtained as a white sublimate (0·24 g., 26%), m. p. 235—240°, shown to be identical with a sample obtained from the natural alkaloid by a mixed m. p. and by the infrared spectra.

γ-Fagarine (VI; R = OMe).— 4-Chloro-8-methoxyfurano(2′ : 3′-2 : 3)quinoline (0·13 g.) in methanolic sodium methoxide [from sodium (0·13 g.) and methanol (3 c.c.)] was heated under reflux for 2 hr. After removal of methanol and addition of water, the mixture was extracted with chloroform. Evaporation of the chloroform and washing the residue with ether furnished a *substance* (0·044 g., 30%) separating from ethanol in colourless plates, m. p. 195—199° (Found : C, 56·0; H, 5·2; Cl, 11·7; OMe, 23·6. $C_{13}H_{14}O_3NCl,\frac{1}{2}H_2O$ requires C, 56·4; H, 5·5; Cl, 12·8; 2OMe, 22·4%), insoluble in aqueous sodium hydroxide and giving no colour with ferric chloride.

Evaporation of the ether washings gave a yellow gum which was chromatographed in benzene on alumina. Elution with benzene–chloroform (4 : 1) gave *γ-fagarine* (0·025 g., 20%), m. p. 127—141°, crystallising from light petroleum (b. p. 60—80°) in pale yellow prisms, m. p. 138—140° alone or mixed with the natural alkaloid (Found : C, 68·1; H, 4·9. $C_{13}H_{11}O_3N$ requires C, 68·1; H, 4·8%). The ultraviolet spectrum [$\lambda_{max.}$ 308 (log ε 3·87), 323 (log ε 3·85), 334 mμ (log ε 3·79)] was identical with that of an authentic sample, as was also the infrared spectrum.

The *picrate*, prepared in ether, separated from ethanol in yellow plates, m. p. 172—173° (lit.,[17] m. p. 176°) (Found : C, 49·8; H, 3·1; N, 12·5. $C_{19}H_{14}O_{10}N_4$ requires C, 49·8; H, 3·1; N, 12·2%).

4′ : 5′-*Dihydro-2-methoxyfurano*(3′ : 2′-3 : 4)*quinoline* (IX; R = H, R′ = OMe).—2-Chloro-4′ : 5′-dihydrofurano(3′ : 2′-3 : 4)quinoline (0·17 g.) in methanol was refluxed with sodium methoxide [from sodium (0·17 g.)] for 2 hr. After evaporation, water was added and the mixture extracted with ether. Evaporation of the ether gave the *dihydromethoxyfurano-quinoline* as a colourless oil which crystallised in needles (0·12 g., 67%), m. p. 77—81°, and separated from light petroleum (b. p. 40—60°) in colourless plates, m. p. 81—82° (Found : C, 71·9; H, 5·3; OMe, 15·2. $C_{12}H_{11}O_2N$ requires C, 71·6; H, 5·5; 1OMe, 15·4%).

2-*Chloro-8-methoxyfurano*(3′ : 2′-3 : 4)*quinoline* (VII; R = Cl).—A solution of 1 : 2-dihydro-8-methoxy-2-oxofurano(3′ : 2′-3 : 4)quinoline (0·08 g.) in phosphorus oxychloride was refluxed for 1 hr., the excess of reagent removed, and water added. The precipitate of the *chlorofurano-quinoline* (0·059 g., 68%) crystallised from ethanol (charcoal) in colourless needles, m. p. 133—134° (Found : C, 61·9; H, 3·4. $C_{12}H_8O_2NCl$ requires C, 61·7; H, 3·5%).

2 : 8-*Dimethoxyfurano*(3′ : 2′-3 : 4)*quinoline* (VII; R = OMe).—Reaction of 2-chloro-8-methoxyfurano(3′ : 2′-3 : 4)quinoline (0·2 g.) with sodium methoxide gave the *dimethoxy-derivative* in pale yellow needles (0·197 g., 98%), m. p. 162—163°, unaffected by crystallisation

[17] Deulofeu, Labriola, and de Langhe, *J. Amer. Chem. Soc.*, 1942, **64**, 2326.

from light petroleum (b. p. 60—80°) (Found: C, 68·4; H, 4·8; N, 6·1. $C_{13}H_{11}O_3N$ requires C, 68·1; H, 4·8; N, 6·1%).

Furano(2′ : 3′-2 : 3)*quinoline* (XIII).—A mixture of 4-chlorofurano(2′ : 3′-2 : 3)quinoline (0·98 g.), 90% hydrazine hydrate (2 c.c.), and ethanol (6 c.c.) was heated under reflux for 3 hr. Complete evaporation gave a yellow solid, m. p. 225—235° (decomp.), which was refluxed with 10% aqueous copper sulphate (30 c.c.) for 1 hr. The solution was made strongly alkaline with aqueous sodium hydroxide and extracted with ether. Evaporation of the ether gave the *furanoquinoline* (0·192 g., 23%), crystallising from light petroleum (b. p. 40—60°) in colourless needles, m. p. 76—77° (Found: C, 78·2; H, 3·9; N, 8·1. $C_{11}H_7ON$ requires C, 78·1; H, 4·2; N, 8·3%).

Potassium Permanganate Oxidation of Furano(2′ : 3′-2 : 3)*quinoline*.—A solution of potassium permanganate (0·6 g.) in acetone (28 c.c.) was added during 1½ hr. to furano(2′ : 3′-2 : 3)-quinoline (0·2 g.) in acetone (10 c.c.). After the addition of water, the solution was clarified with sulphur dioxide, and the acetone removed by evaporation. 3-Carboxy-2-hydroxyquinoline slowly crystallised as a yellow solid (0·06 g., 27%), separating from ethanol in pale yellow needles, m. p. 300—312° (Found: C, 63·3; H, 3·4. Calc. for $C_{10}H_7O_3N$: C, 63·5; H, 3·7%). The product was identical (mixed m. p. and ultraviolet and infrared spectra) with a sample (m. p. 300—312°) prepared by Friedlander and Goering's method.[18]

3-2′-*Ethoxyethyl*-2 : 4-*dihydroxy*-8-*methoxyquinoline* (XVII).—The crude product (31·7 g.) was obtained from *o*-anisidine (28·9 g.) as described previously. A chloroform solution was shaken with several portions of 2N-aqueous sodium hydroxide, dried, and evaporated, to give 1 : 2 : 4′ : 5′-tetrahydro-8-methoxy-2-oxofurano(3′ : 2′-3 : 4)quinoline, separating from ethanol in prisms (3·79 g., 7%), m. p. and mixed m. p. 218—220°. The alkaline washings were acidified and extracted with chloroform. Evaporation of the chloroform solution gave the dihydroxy-compound in pale brown prisms (23·8 g., 39%), m. p. and mixed m. p. 123—130°, sufficiently pure for use in subsequent reactions.

3-2′-*Ethoxyethyl*-1 : 2-*dihydro*-4 : 8-*dimethoxy*-2-*oxoquinoline* (XVIII).—3-2′-Ethoxyethyl-2 : 4-dihydroxy-8-methoxyquinoline (2·2 g.), suspended in ether (200 c.c.) containing a few drops of methanol, was treated with excess of ethereal diazomethane. After 12 hr. at room temperature, the solvent was evaporated and the residue dissolved in ether (50 c.c.). When the solution was concentrated to 25 c.c. the *dimethoxyquinoline* was deposited as colourless plates (1·0 g.), m. p. 119—120°, and a further quantity (0·32 g.), m. p. 115—118°, was obtained by concentration of the ether solution (total 1·32 g., 57%). Crystallisation from aqueous methanol gave plates, m. p. 122—123° (Found: C, 65·0; H, 6·6. $C_{15}H_{19}O_4N$ requires C, 65·0; H, 6·9%).

2 : 4-*Dichloro*-3-2′-*ethoxyethyl*-8-*methoxyquinoline* (XIX).—3-2′-Ethoxyethyl-2 : 4-dihydroxy-8-methoxyquinoline (20 g.) and phosphorus oxychloride (200 c.c.) were refluxed for 1 hr. and the excess of reagent removed. Addition of water gave the *dichloro-compound* (22·14 g., 99%), separating from aqueous ethanol in needles, m. p. 73—74° (Found: C, 56·0; H, 4·9; Cl, 23·8. $C_{14}H_{15}O_2NCl_2$ requires C, 56·0; H, 5·0; Cl, 23·6%).

4-*Chloro*-3-2′-*ethoxyethyl*-1 : 2-*dihydro*-8-*methoxy*-2-*oxoquinoline* (XX; R = OEt).—The above dichloro-compound (1·16 g.), 6N-hydrochloric acid (28 c.c.), and dioxan (20 c.c.) were heated under reflux for 2½ hr. and kept at room temperature for 12 hr. The crystalline precipitate (0·7 g., 65%), m. p. 159—160°, of the *chloroquinolone* was purified by chromatography on alumina. Elution with chloroform, evaporation, and crystallisation from ethanol gave needles, m. p. 162—163° (Found: C, 59·8; H, 5·6; N, 5·4; Cl, 12·3. $C_{18}H_{16}O_3NCl$ requires C, 59·7; H, 5·7; N, 5·0; Cl, 12·6%).

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[18] Friedlander and Goering, *Ber.*, 1884, **17**, 459.

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418. *The Formation of Iodine Cations. Part II.*[1] *Spectroscopic Evidence.*

By M. C. R. Symons.

The visible and ultraviolet absorption spectra of blue solutions of iodine in concentrated oleums are presented and compared with the spectra of solutions of iodine in dilute oleums and in sulphuric acid. The blue solutions are characterised by an intense band at 650 mμ, which is identified tentatively as a triplet–singlet transition of the iodine cation, since the results obtained from this ion in emission show that such a band should occur in this region. A small band at 1400 mμ may also be caused by the iodine cation but relatively weak bands at 470, 400, and 300 mμ are shown to be caused by two other absorbing species. Aspects of the spectroscopic, magnetic, and chemical properties of ter- and quinque-valent iodine in these solvents are reported.

It was postulated in Part I [1] that the paramagnetic species present in blue solutions obtained when iodine reacts with concentrated oleum is the free iodine cation, I^+. Although this ion does not seem to have been studied before in solution it has been known for some time that it is present in electronically excited states when iodine vapour is decomposed by an electric arc.[2,3] From the observed transitions between excited states, Murakawa [3] has calculated the energies of the low-lying states relative to the ground state, although transitions between these levels have not been directly observed. The spectroscopic terms for the ground and low-lying excited states together with the wavelengths expected for transitions from the ground state to these levels are recorded in the Table.

Low-lying excited states for the iodine cation.

Orbital type	$^3P_2$	$^3P_1$	$^3P_0$	$^1D_2$	$^1S_0$
Energy (cm.$^{-1}$)	153,362	146,272	146,911	139,631	120,733
Transitions	$^3P_2 \longrightarrow {}^3P_1$	$^3P_2 \longrightarrow {}^3P_0$	$^3P_2 \longrightarrow {}^1D_2$	$^3P_2 \longrightarrow {}^1S_0$	
Wavelength (mμ)	1410	1550	728	310	

All these transitions are forbidden by atomic selection rules. The first permitted transitions lie below 200 mμ and therefore cannot be studied when sulphuric acid is the solvent. However, for elements of high atomic number, triplet–singlet transitions of moderate intensity are observed and therefore the $^3P_2 \longrightarrow {}^1D_2$ transition should be readily detectable. Of the others, only the $^3P_2 \longrightarrow {}^3P_1$ transition is likely to be detectable, and even this should be extremely weak. Therefore solutions containing the free iodine cation should appear blue.

The spectrum of the blue solution in oleum is characterised by a strong band with a maximum at 650 mμ (Fig. 3), the intensity being about double that of the 520 mμ band of the iodine molecule. It is postulated that this band is the expected $^3P_2 \longrightarrow {}^1D_2$ transition of the iodine cation shifted to shorter wavelengths by solvent interaction. A small band in the infrared region with a maximum at about 1400 mμ (not recorded in Fig. 3) may also be caused by the iodine cation but the bands at 470, 400, and 300 mμ cannot be caused by the free cation if the energy-level scheme given in the Table is correct. However, it was postulated in Part I that only part of the iodine is present as the cation, since the observed paramagnetism was somewhat smaller than that expected for I^+. Analysis showed that most of the iodine was in the univalent state, although the possibility that zero and ter-valent iodine compounds were present in equivalent amounts was not excluded. In

[1] Part I, Symons, *J.*, 1957, 387.
[2] Tolansky, *Proc. Roy. Soc.*, 1935, *A*, **149**, 269.
[3] Murakawa, *Z. Physik*, 1938, **109**, 162.

particular, it was suggested that the ion ISO_3^+ might be present, and that covalent bonding might occur between the iodine cation and ions such as HSO_4^-, $HS_2O_7^-$, etc.

That the bands at 470, 400, and 300 mμ are not directly related to the 650 mμ band can be seen by comparing the results recorded in Figs. 1 and 3. Thus the 650 and 400 mμ bands are not observed in brown solutions of iodine in dilute oleums, but the 470 and 300

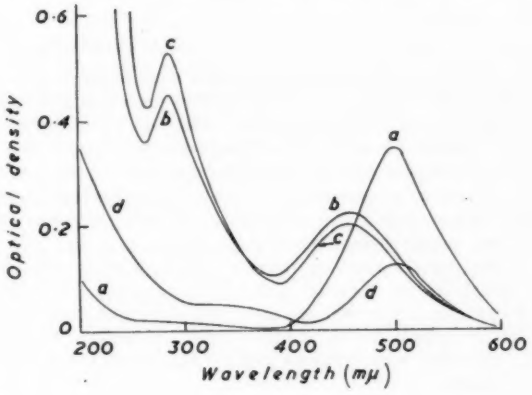
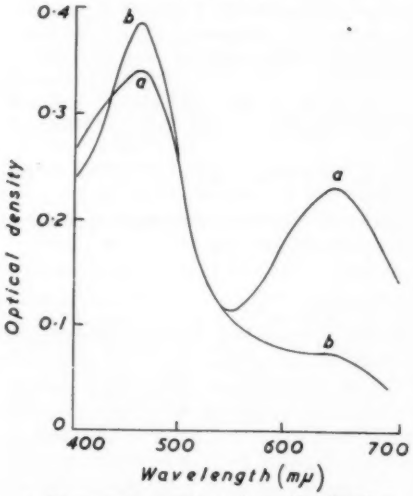


FIG. 1. *Spectra of solutions of iodine in sulphuric acid and dilute oleums.*

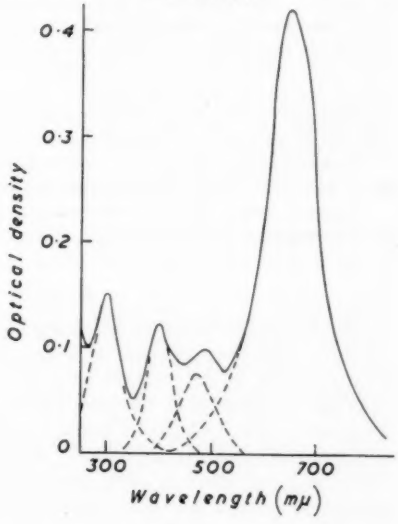
a, In sulphuric acid (98·4%); *b*, freshly prepared solution in oleum (2%); *c*, same solution immediately after prolonged heating; *d*, same solution after 4 hr. at room temperature.

FIG. 2. *Effect of heat on the spectrum of iodine in oleum* (10%).



a, At room temperature, immediately after heating; *b*, same solution after 12 hr.

FIG. 3. *Spectrum of iodine in concentrated oleum* (65%).



mμ bands are still present. When sulphur trioxide is added to a solution in dilute oleum these bands decrease, and the 650 and 400 mμ bands increase in intensity (Fig. 2). The 400 mμ band is only found together with the 650 mμ band, but when a blue solution is heated the latter band gains in intensity at the expense of the former, and this effect is reversed on cooling. Such behaviour is not normally observed for two transitions of the some compound and it is accordingly concluded that the 400 mμ band is caused by a third component.

The main conclusions are that these results in no way disprove the theory that free iodine cations are present in large concentration in solutions of iodine in concentrated oleum,[1] and that the proximity of the main 650 mμ band to the expected $^3P_2 \longrightarrow {}^1D_2$ transition of the cation supports the theory. Other features of these solutions, together with some properties of solutions of ter- and quinque-valent iodine (I^{III} and I^{V} respectively) in these solvents, are reported and discussed below.

Experimental

Spectrophotometric measurements were made with a Unicam SP500 quartz spectrophotometer (below 360 mμ), a Unicam SP600 glass spectrophotometer (360—900 mμ), and a Hilger Uvispek spectrophotometer (900—1600 mμ). All cells were calibrated, and controls were prepared from the same oleum used for solutions. 1 cm. cells were stoppered, but 1 mm. cells were not covered since it was found that when moisture was absorbed from the atmosphere a thin upper layer was formed which did not affect the optical density of the solution and effectively sealed off the contents of the cell. 0·1 mm. cells were obtained by the insertion of 0·9 mm. quartz spacers into 1 mm. cells.

Cells were cleaned by repeated washing with test solutions and care was taken to avoid striations in the solution since their presence seriously affected ultraviolet measurements. For readings above 900 mμ thin cells were used and a Chance OX2 infrared filter inserted in order to reduce effects of stray light. However, relatively large slit-widths were necessary and therefore little reliance can be placed on the precise optical-density values obtained in this region.

High-temperature measurements were made by pouring hot solutions into pre-heated cells, stoppering, and rapidly recording the relevant optical densities. The resulting values were compared with the spectrum of the cold solution. Iodine and solvents were purified as described in Part I.[1] Solutions of iodyl sulphate were prepared either by heating " AnalaR " potassium iodate in concentrated sulphuric acid or by heating equivalent portions of iodine and iodine pentoxide suspended in sulphuric acid.[4] The yellow crystalline product was dissolved in sulphuric acid or oleum for spectrophotometric measurements. Aqueous solutions containing protonated hypoiodous acid, H_3OI^+, were prepared as described by Bell and Gelles.[5] Solutions containing I^{V} were prepared by shaking finely powdered potassium iodate or iodine pentoxide with sulphuric acid or oleum at room temperature.

Oleum concentrations were estimated by Kunzler's " fog–clear " method,[6] which is easy and rapid, and sufficiently accurate for most purposes.

Magnetic measurements were made as described in Part I [1] for both concentrated solutions of iodyl sulphate and the solid.

Results and Discussion

Spectra of Solutions in Sulphuric Acid and Dilute Oleums (*Fig.* 1).—In concentrated sulphuric acid the spectrum of iodine is close to that of the vapour (curve *a*) and there appears to be no interaction with the solvent. This result agrees with those already reported [7,8] except that the broad peak at 320 mμ reported by Bower and Scott [8] was not observed. The solubility of iodine in dilute oleum is very much greater than in sulphuric acid and the solutions are brown. A typical spectrum is curve *b*. Curve *c* was obtained from the same solution after prolonged heating to remove sulphur trioxide so that its concentration was less than that in 100% sulphuric acid. Iodine was lost during this process and the optical-density scales have been adjusted to facilitate comparison. This spectrum underwent a marked change over a period of about 4 hr., and curve *d* represents the final result.

The appearance of a new peak at 300 mμ, and the shift of the main iodine transition

[4] Masson and Argument, *J.*, 1938, 1702.
[5] Bell and Gelles, *J.*, 1951, 2734.
[6] Kunzler, *Analyt. Chem.*, 1953, **25**, 193.
[7] Buckles and Mills, *J. Amer. Chem. Soc.*, 1953, **75**, 552.
[8] Bower and Scott, *ibid.*, p. 3583.

towards the ultraviolet are changes which resemble the effect of " donor " solvents on the iodine spectrum. However, it is probably the iodine molecule which is now acting as donor, and it is postulated that the new complex is the ion I_3^+, formed by partial oxidation of the element. Masson [9] has already presented arguments which point to the presence of I_3^+ and even I_5^+. By analogy with chlorine monoxide, the ion I_3^+ would be bent and diamagnetic, and a series of relatively low-energy transitions would be expected.

If I_3^+ is formed by the reaction $I_2 + I^+ \rightleftharpoons I_3^+$, it should be possible to influence the position of equilibrium by suitable operations. Thus when the concentration of iodine is large no free I^+ should be present and therefore the 650 mμ band should be absent, and when the concentration of I^+ is large there should be no free iodine. Qualitatively, these expectations seem to be correct, but quantitative measurements are difficult because the bands are shifted and their intensities altered by overlap with the edges of neighbouring bands. This concept is supported by the qualitative appearance of the 650 mμ band in these solutions at high temperatures. On heating, the brown colour changes to a colour corresponding to the superposition of violet and blue: a colour which corresponds very closely to that expected for a mixture of uncomplexed iodine and the iodine cation. Rapid cooling causes the immediate return of the original brown colour. It is suggested that I_3^+ dissociates into I^+ and iodine at high temperatures.

The slow change in the spectrum when the concentration of sulphur trioxide is reduced to a value corresponding to less than 100% sulphuric acid (Fig. 1, curve *c* ⟶ curve *d*) shows that if this theory is correct, I_3^+ decomposes very slowly. The resulting violet solution has a much greater ultraviolet absorption than a pure iodine solution (compare curves *a* and *d*). This new absorption resembles that of I^{III} in sulphuric acid (see later) and it is accordingly postulated that I_3^+ decomposes to give I^{III} and iodine.

In order to check the possibility that the new peak at 300 mμ is caused by dissolved sulphur dioxide, the spectra of solutions of sulphur dioxide in sulphuric acid and oleum were measured. In each case a strong band at 280 mμ was observed, the absorption at 300 mμ being small.

Spectra of Solutions in Concentrated Oleums.—The effect of an increase in the concentration of sulphur trioxide on the absorption spectra is presented in Figs. 2 and 3. The spectra recorded in Fig. 2 show how the 650 mμ band grows at the expense of the 470 mμ band. The slight shoulder at 400 mμ in curve *a* is probably caused by the 400 mμ band which appears in concentrated oleum (Fig. 3).

When the brown solution obtained by dissolving iodine in 10% oleum was warmed to 50° the colour changed to green. It remained green when the solution was cooled (Fig. 2, curve *a*) but reverted to brown after several hours (curve *b*). If the 650 mμ band is caused by the iodine cation (and for ease of presentation this assumption will be made in the following discussion) then its formation is facilitated by an increase in temperature and, in this solvent, the process by which it is destroyed is very slow at room temperature. This decomposition is evidently a disproportionation to give I_3^+ and tervalent iodine.

Fig. 3 represents an attempt to break down the overall spectrum of the blue solutions into its component bands (broken lines). Further increase in the concentration of oleum has only a minor effect on this spectrum, and an equilibrium appears to have been reached. It is reasonably certain that the 470 and 300 mμ bands are the same as are found in dilute oleum and it is accordingly postulated that there is still some residual I_3^+ in these solutions. An approximate estimate based on relative band-heights shows that I_3^+ comprises about 10% of the total iodine in the solution.

Identification of the compound responsible for the 400 mμ band is impossible at present.

Spectra of Protonated Hypoiodous Acid and of Ter- and Quinque-valent Iodine.—Quantitative measurements of these spectra are as yet incomplete, but the following qualitative features are relevant. In no instance has any well-defined peak been observed. Aqueous solutions of protonated hypoiodous acid were straw-yellow, and the slowly rising

[9] Masson, *J.*, 1938, 1708.

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ultraviolet absorption showed a slight point of inflection in the 310 mμ region. Tervalent iodine solutions obtained from crystalline yellow iodyl sulphate had identical spectra in sulphuric acid and oleum. Absorption begins at about 450 mμ, levels out to a plateau in the 330 mμ region, and rises steeply below 300 mμ, thus closely resembling the low-wavelength portion of curve *d*, Fig. 1. Much evidence in favour of the formulation IO^+ for this yellow I^{III} species has been advanced.[4] Unfortunately the spectrum described is so ill defined that it sheds no light on this matter. By analogy with oxygen it was thought that the ground state of this ion might be $^3\Sigma$ and therefore that it would be paramagnetic. Magnetic-susceptibility measurements on solid iodyl sulphate and on concentrated solutions in sulphuric acid and oleum show that no paramagnetic material is present. It must accordingly be concluded either that IO^+ is not paramagnetic or that IO^+ is not present in these compounds. Significant to this discussion is the observation that solid iodine dioxide is diamagnetic.[10] It has been suggested that this oxide is ionic, having the structure IO^+,IO_3^-: if this is correct then it must be concluded that the iodyl ion IO^+ is not paramagnetic.

Quinquevalent iodine compounds dissolve in sulphuric acid and oleum to give colourless solutions having ultraviolet spectra similar to that of the iodate ion, although the long-wavelength edge is nearer the visible region. Since both sulphur dioxide and nitrite ions have a pronounced absorption peak in the 300 mμ region it was hoped that if the I^V compound in these solutions were IO_2^+ then a similar band would be detected. In the absence of such a band no identification of the absorbing species can be made.

Reactivity.—Quinquevalent iodine in sulphuric acid and oleum readily decomposes to tervalent iodine and oxygen when heated. In concentrated oleum the I^{III} compound decomposes further and a green solution containing a mixture of I^{III} and I^+ results. Iodine and I^V in sulphuric acid react immediately to form I^{III} at room temperature. In contrast, I^V and I^+ in oleum do not react at room temperature, but I^{III} is formed slowly when the solution is heated.

When solutions of I^{III} and sulphur sesquioxide in oleum are mixed, sulphur dioxide is evolved and the 590 mμ band of sulphur sesquioxide is replaced by the 650 mμ band attributed to the iodine cation:

$$IO^+ + S_2O_3 \longrightarrow I^+ + 2SO_2$$

This reaction is rapid at room temperature, and should be compared with the conclusions drawn by Masson [4,9] that iodine reduces oleum to sulphur sesquioxide and is itself oxidised to the tervalent state.

Addition of potassium hydrogen sulphate to a blue solution does not alter the relative heights of the visible bands but there is a marked increase in absorption in the ultraviolet. Potassium hydrogen sulphate acts as a base in this solvent, and reacts with sulphur trioxide to form KHS_2O_7 and possibly trimeric or polymeric sulphate. Co-ordination of the iodine cation with the resulting negative ions may result in the formation of a compound which has a rising ultraviolet absorption, or the formation of such a compound may facilitate the production of tervalent iodine:

$$I^+ + HS_2O_7^- \rightleftharpoons [IO{-}SO_2{-}SO_4H] \longrightarrow IO^+ + SO_2 + HSO_4^-.$$

Clearly, either of these interpretations would explain the decrease in paramagnetism which results when potassium hydrogen sulphate is added.[1]

Thanks are offered to Dr. D. Schonland for helpful advice.

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[10] Willmarth and Dharmatti, *J. Amer. Chem. Soc.*, 1950, **72**, 5789.

419. *Methylene Derivatives of* L-*Fucose.*

By R. L. Nelson and Elizabeth Percival.

L-Fucose on treatment with paraformaldehyde yielded five methylene derivatives. Three of these have been separated and characterised as a di-*O*-methylene-L-fucose, and two mono-*O*-methylene-L-fucoses. 2-*O*-Methyl-L-fucose has been synthesised from methyl 3 : 4-*O*-*iso*propylidene-α-L-fucoside.

L-Fucose when treated with paraformaldehyde according to the method of Andrews, Hough, and Jones [1] gave chromatographic evidence that at least four compounds were formed. Crystals (I) were obtained from a rapidly-obtained chloroform extract of the neutralised product. The residual material, after further treatment with paraldehyde, was separated on cellulose into four fractions, and two of these fractions (III and IV) were investigated.

The crystals (I) (39·7% yield) which could not be detected on the paper chromatogram were non-reducing to Fehling solution and on hydrolysis gave L-fucose and 1·9 mol. of formaldehyde. They gave correct analytical results for a di-*O*-methylenefucose and on partial acid hydrolysis gave a mixture of L-fucose and fraction (IV). Separation on thick paper gave crystalline fraction (IV).

Fraction (IV) a mono-*O*-methylenefucose, was reducing and gave one mol. of formaldehyde on hydrolysis. Oxidation with periodate gave an uptake of 0·93 mol. of periodate and a release of 0·88 mol. of formic acid. Methylation and hydrolysis followed by separation on thick paper led to isolation of 2-*O*-methyl-L-fucose. Fraction (IV) must therefore be either the 3 : 5- or the 3 : 4-mono-*O*-methylene-L-fucose. Its high negative rotation ($[\alpha]_D^{20}$ −95°) is suggestive of a pyranose ring {cf. 2 : 3 : 4-tri-*O*-methyl-L-fucose, $[\alpha]_D$ −128°; [2] 2 : 3 : 5-tri-*O*-methyl-L-fucose, $[\alpha]_D^{20}$ +70° (*c*, 1·7 in H_2O) (unpublished work)}. If fraction (IV) is the 3 : 4-mono-*O*-methylene-L-fucose and not the 3 : 5-isomer, then fraction (I) is 1 : 2-3 : 4-di-*O*-methylene-L-fucose.

Fraction (III) was a reducing syrup; it gave approximately 1 mol. of formaldehyde on hydrolysis and was unaffected by periodate. Methylation followed by hydrolysis yielded a syrup which was shown to contain fucose, 3-*O*-methylfucose, and a substance with an R_F value slightly lower than that of 2 : 3 : 4-tri-*O*-methylfucose (paper chromatography). It would appear that the methylene group had been partly removed during methylation, and fraction (III) is tentatively identified as 2 : 5-mono-*O*-methylene-L-fucose.

Although fractions (II) and (V) were insufficient for complete investigation they both appeared to be mono-*O*-methylene derivatives. In contrast to rhamnose [1] no evidence for the presence of *O*-dimethyleneoxy-compounds was obtained.

Authentic crystalline 2-*O*-methyl-L-fucose has been synthesised from methyl 3 : 4-*O*-*iso*propylidene-α-L-fucoside by methylation followed by hydrolysis.

Experimental

Chromatography was carried out by the descending method on Whatman No. 1 filter paper, butane-1-ol–ethanol–water (40 : 11 : 19 v/v; upper layer) being used as mobile phase. L-Fucose and its derivatives were located on the chromatogram by spraying it with aniline oxalate. The rate of movement of compounds on the chromatogram is quoted relative to that of the solvent front (R_F value) and to that of L-fucose (R_{Fu} value).

Preparation of the Methylene Derivatives.—L-Fucose ($[\alpha]_D$ −74·5° in H_2O) (15 g.) was treated with paraformaldehyde according to the method of Andrews, Hough, and Jones.[1] After neutralisation with barium carbonate, the filtrate was rapidly extracted with chloroform (3 × 50 c.c.). The chloroform extracts were dried ($MgSO_4$) and evaporated to a syrup which was dissolved in water and rapidly extracted with chloroform. The chloroform extracts on

[1] Andrews, Hough, and Jones, *J. Amer. Chem. Soc.*, 1955, **77**, 125.
[2] O. T. Schmidt, Mayer, and Distelmaier, *Annalen*, 1943, **555**, 26.

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concentration gave crystals (3·3 g.) of material which could not be detected on the paper chromatogram. Recrystallisation from ethanol and sublimation afforded *di*-O-*methylene*-L-*fucose* (I), m. p. 77°, $[\alpha]_D$ +58° (*c*, 0·7 in MeOH), +68° (*c*, 0·87 in H_2O) (Found: C, 51·3; H, 6·3. $C_8H_{12}O_5$ requires C, 51·1; H, 6·4%). The combined aqueous residues were extracted with chloroform during 18 hr. with continuous shaking. Evaporation of the dried ($MgSO_4$) chloroform extracts gave a syrup (*A*). This syrup smelled strongly of formaldehyde and trioxan sublimed from it when it was heated under reduced pressure. Chromatographic examination showed the presence of compounds with R_F 0·80, R_{Fu} 3·5 (II); R_F 0·70, R_{Fu} 3·0 (III); R_F 0·60, R_{Fu} 2·4 (IV). Continuous extraction of the aqueous mother liquors with chloroform for a further 24 hr. yielded a syrup (*B*) which on chromatographic examination was shown to contain fractions (III) and (IV) with a trace of a compound (V), R_F 0·50. The aqueous mother liquors on evaporation gave a yellow syrup consisting mainly of fucose (chromatography). This syrup together with fucose (2 g.) was treated with paraformaldehyde as before.[1] More of fraction (I) (3·6 g.) (total yield 6·9 g. from 17 g. of fucose) was obtained. The aqueous solution on evaporation gave a yellow syrup (*C*).

Syrups *A*, *B*, and *C* were combined and a portion (*ca.* 5 g.) was fractionated on a cellulose column with light petroleum (b. p. 100—120°)–butane-1-ol (70 : 30, changed in stages to 40 : 60 parts v/v) as the mobile phase; finally the fucose was eluted with ethanol. The following fractions were collected and treated with charcoal: (II) Crystalline (37 mg.), $[\alpha]_D^{20}$ +12° (*c*, 0·37 in H_2O), non-reducing to Fehling solution. (IIa) Syrup (26 mg.), a mixture of (II) and (III). (III) Syrup (248 mg.), $[\alpha]_D^{25}$ +16°, reducing. (IV) Crystalline (677 mg.), m. p. 96°, reducing to Fehling solution, $[\alpha]_D$ −124° (2 min.) ⟶ −90·5° (const., *c*, 5·8 in H_2O) (Found: C, 47·6; H, 6·7. $C_7H_{12}O_5$ requires C, 47·7; H, 6·8%). (V) (25 mg.), $[\alpha]_D$ −64° (*c*, 0·25 in H_2O).

Hydrolysis of the Methylene Derivatives.—The crystalline derivatives and the syrups were hydrolysed with N-sulphuric acid at 100° for 2 hr. [2N-H_2SO_4; 4 hr. for fraction (I)] giving fucose (detected chromatographically) and formaldehyde. In each case, formaldehyde was identified and estimated according to the method used by Andrews, Hough, and Jones.[1] Results are given in Table 1.

TABLE 1.

Compound or fraction	I	II	IIa	III	IV	V
M (calc.)	188	176	176	176	176	176
Wt. taken (mg.)	10·89	9·2	13	9·5	10·9	12·3
Yield of dimedone deriv. (mg.)	31·6	10·0	20·4	13·4	17·8	17·6
Yield of formaldehyde (mol.)	1·90	0·66	0·95	0·86	1·0	0·86

Periodate Oxidation.—To each compound (5—10 mg.) in water (5 c.c.) 0·2N-sodium metaperiodate (2 c.c.) was added, and the mixture was set aside in the dark. After 3 hr. the reaction mixture was treated according to one of the following methods: (i) Boric acid (2 g.) and saturated borax (5 ml.) were added and the mixture was set aside (3 min.). Potassium iodide (5 ml., 40%) was then added and the solution titrated with sodium arsenite. (ii) Ethylene glycol (1 c.c.) was added, and the formic acid liberated was titrated with 0·01N-sodium hydroxide. In order to hydrolyse the formyl esters which had been produced the formic acid titrations were completed on hot solutions. Results are given in Table 2.

TABLE 2.

Compound or fraction	II	III	IV	Compound or fraction	II	III	IV
M (calc.)	176	176	176	Wt. taken (mg.)	9·0	9·5	7·70
Wt. taken (mg.)	9·0	9·5	6·8	Formic acid yield (c.c. of			
Periodate uptake (c.c. of 0·01N)	2·73	2·2	7·10	0·01N)	nil	0·5	3·0
" (mol.)	0·25	0·19	0·93	" " (mol.)	nil	0·13	0·88

Partial Hydrolysis of Di-O-*methylene*-L-*fucose* (I).—The compound (333 mg.) was heated at 100° in 0·01N-sulphuric acid and the hydrolysis followed polarimetrically: $[\alpha]_D$ +225° (initial), +219° (15 min.), +210° (2 hr.). The concentration of acid was increased to 0·02N and heating continued. The rotations observed were +180° (5 hr.), +141° (10 hr.), +110° (13 hr.). Aliquot portions were removed after (*a*) 5 hr., (*b*) 10 hr., and (*c*) 13 hr. Neutralisation, concentration, and chromatographic examination showed (*a*) a single faint spot, R_F 0·60, R_{Fu} 0·24 (cf. fraction IV), (*b*) a spot R_F 0·60, and a faint spot corresponding to fucose, (*c*) the same two

spots as (*b*). The remaining solution afforded a syrup after cooling, neutralisation ($BaCO_3$), and concentration. Separation of this syrup on thick paper gave two fractions: (1) R_F 0·60, R_{Fu} 0·24, crystalline, m. p. and mixed m. p. with compound (IV) 96°, $[\alpha]_D^{18}$ −95° (*c*, 0·25 in H_2O); (2) crystalline fucose, m. p. 140—142°.

Fraction (III).—This syrup (100 mg.) was methylated thrice with Purdie reagents. Hydrolysis with N-sulphuric acid for 2 hr., neutralisation ($BaCO_3$), and concentration gave a syrup (48 mg.) which gave spots corresponding to fucose (trace), 3-*O*-methylfucose, and a dark red spot with R_F 0·66 [cf. 2 : 3 : 4-tri-*O*-methylfucose, R_f 0·70; 2 : 3 : 5-tri-*O*-methylfucose, R_F 0·87 (unpublished work)] similar in colour to other spots given by fucofuranose derivatives.

3 : 4-O-*Methylene*-L-*fucose* (IV).—This compound (280 mg.) was methylated thrice with Purdie reagents. The addition of methanol (2 c.c.) was necessary to dissolve the material in the first methylation. The product, a syrup (n_D^{18} 1·4650), was hydrolysed for 1 hr. with N-sulphuric acid at 100° and the neutralised solution ($BaCO_3$) filtered and concentrated to syrup. Chromatographic examination showed this to be 2-*O*-methylfucose contaminated with a trace of fucose. Separation on thick paper gave crystalline 2-*O*-methyl-L-fucose, m. p. and mixed m. p. 150°.

Synthesis of 2-O-*Methylfucose* (With Miss B. Guarco).—Methyl 3 : 4-*O*-*iso*propylidene-α-L-fucoside was prepared by Percival and Percival's method [3] from L-fucose. Four methylations with Purdie reagents followed by distillation (bath temp. 90—100°/0·04 mm.) gave a syrup, n_D^{16} 1·4555°. Hydrolysis with 4% sulphuric acid at 100° for 6 hr. afforded crystalline 2-O-*methylfucose*, m. p. 150—152°, $[\alpha]_D^{18}$ −87° (*c*, 1·0 in H_2O) (Found: C, 48·0; H, 7·6; OMe, 17·55. $C_7H_{14}O_5$ requires C, 47·2; H, 7·8; OMe, 17·4%).

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Department of Chemistry, University of Edinburgh. [*Received, January 7th*, 1957.]

[3] Percival and Percival, *J.*, 1950, 690.

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420. *Addition of Free Radicals to Unsaturated Systems. Part XIII.* Direction of Radical Addition to Chloro-1 : 1-difluoroethylene.*

By R. N. Haszeldine and B. R. Steele.

Free-radical attack on chloro-1 : 1-difluoroethylene is predominantly and probably exclusively on the CF_2 group. Photochemical reaction of the olefin with trifluoroiodomethane yields the compound $CF_3{\cdot}CF_2{\cdot}CHClI$ and with hydrogen bromide the compound $CF_2Br{\cdot}CH_2Cl$; structures are proved. The polarisation of the olefin during reactions involving ionic intermediates is $\overset{\delta+}{C}F_2{:}\overset{\delta-}{C}HCl$. The results are discussed, and an earlier report in the literature is corrected.

Trifluoroiodomethane shows no dark reaction with chloro-1 : 1-difluoroethylene, but irradiation of the mixture with light of wavelength >2200 Å (silica vessels) or >3000 Å (Pyrex vessels) gives a high yield of a compound $CF_3{\cdot}[C_2HClF_2]{\cdot}I$. Only small amounts of hexafluoroethane and chlorotrifluoromethane are formed as by-products by combination of two trifluoromethyl radicals and abstraction of chlorine.

That the main product is 3-chloro-1 : 1 : 1 : 2 : 2-pentafluoro-3-iodopropane (I) formed by attack of the CF_3 radical on the CF_2 group of the olefin, and not the isomer (II), is shown by spectroscopic and chemical evidence.

$CF_3{\cdot}CF_2{\cdot}CHClI$	$CF_3{\cdot}CHCl{\cdot}CF_2I$	$CF_3{\cdot}CF_2{\cdot}CHCl_2$	$CF_3{\cdot}CHCl{\cdot}CF_2Cl$
(I)	(II)	(III)	(IV)

* Part XII, *J.*, 1956, 61.

The maximum in the ultraviolet spectrum of a compound $R{\cdot}CF_2I$ in light petroleum solution varies from 267 mμ when R = alkyl to 271 mμ when R = perfluoroalkyl.[1] The corresponding position for a compound R·CHClI is 278—280 mμ (see Table). There is

Ultraviolet spectra in light petroleum.

	$\lambda_{max.}$	$\varepsilon_{max.}$	$\lambda_{min.}$	$\varepsilon_{min.}$		$\lambda_{max.}$	$\varepsilon_{max.}$	$\lambda_{min.}$	$\varepsilon_{min.}$
$CF_3{\cdot}CF_2{\cdot}CHClI$ ...	280	345	233	70	$CF_2Cl{\cdot}CHClI$	279	260	229	35
$CF_3{\cdot}CHCl{\cdot}CHClI$	280	400	243	150	$CHCl_2{\cdot}CHClI$	278	420	232	55
$CF_2{\cdot}CHF{\cdot}CHClI$	280	400	229	55	$CF_2{\cdot}CH_2{\cdot}CHClI$ ...	278	430	231	40

sufficient difference between these characteristic positions for them to be used diagnostically. The product from the reaction of trifluoroiodomethane and chloro-1 : 1-difluoroethylene has maximum absorption at 280 mμ in light petroleum (Table) and thus contains the R·CHClI chromophore.

Reaction of the 1 : 1 adduct with chlorine gave 3 : 3-dichloro-1 : 1 : 1 : 2 : 2-pentafluoropropane (III); under similar conditions, the halide (II) would have given 1 : 2-dichloro-1 : 1 : 3 : 3 : 3-pentafluoropropane (IV). Compound (III) contains a C_2F_5 group; an authentic specimen, synthesised from pentafluoropropanol, as follows:

$$C_2F_5{\cdot}CH_2{\cdot}OH \longrightarrow C_2F_5{\cdot}CH_2{\cdot}O{\cdot}SO_2{\cdot}C_6H_4Me \xrightarrow{KCl} C_2F_5{\cdot}CH_2Cl \xrightarrow{Cl_2} C_2F_5{\cdot}CHCl_2$$

had an infrared spectrum identical with that of the dichloro-compound obtained from (I). An authentic specimen of the dichloride (IV) was prepared by reaction of chlorine with 1 : 1 : 3 : 3 : 3-pentafluoropropene.[2] The dichlorides (III) and (IV) are readily distinguished by the presence or absence of strong bands in their infrared spectra at 13·18 μ (III) and 11·10 μ (IV).

That the 1 : 1 adduct obtained from trifluoroiodomethane and chloro-1 : 1-difluoroethylene did not contain even traces of isomer (II) was confirmed by its reaction with zinc and ethanol. Under these conditions, compound (II), like (IV), would have given 1 : 1 : 3 : 3 : 3-pentafluoropropene in high yield, but this olefin [2] was not detected spectroscopically. More than 1—2% of (II) present in the original $CF_3{\cdot}[C_2HClF_2]{\cdot}I$ would have been detected by the procedure used. 3-Chloro-1 : 1 : 1 : 2 : 2-pentafluoropropane and 2 : 3 : 3 : 3-tetrafluoropropene were the major products, arising by reduction of the iodine and fluoride elimination:

$$CF_3{\cdot}CF_2{\cdot}CHClI \xrightarrow{Zn} CF_3{\cdot}CF_2{\cdot}CHCl{\cdot}ZnI \xrightarrow{EtOH} CF_3{\cdot}CF_2{\cdot}CH_2Cl$$
$$CF_3{\cdot}CF_2{\cdot}CH_2Cl \longrightarrow CF_3{\cdot}CF_2{\cdot}CH_2{\cdot}ZnCl \longrightarrow CF_3{\cdot}CF_2{\cdot}CH_2^- \longrightarrow F^- + CF_3{\cdot}CF{:}CH_2$$

A control experiment showed that the chloropentafluoropropane reacts with zinc and ethanol under similar conditions to give the tetrafluoropropene. The corresponding iodo-compound gives a high yield of the tetrafluoropropene ($C_2F_5{\cdot}CH_2I \longrightarrow CF_3{\cdot}CF{:}CH_2$).

Hydrogen bromide does not react with chloro-1 : 1-difluoroethylene in the dark at room temperature; the rapid reaction occurring on irradiation (>2200 Å) yields 1-bromo-2-chloro-1 : 1-difluoroethane (V) quantitatively. The structure of this was proved by its ready de-

$CF_2Br{\cdot}CH_2Cl$	$CHF_2{\cdot}CHClBr$	$CF_2Cl{\cdot}CH_2Cl$	$CF_2{\cdot}CH_2Cl$
(V)	(VI)	(VII)	(VIII)

halogenation, on treatment with zinc and ethanol, to 1 : 1-difluoroethylene [1] in high yield; the other possible product, (VI), could not yield difluoroethylene in this way. Attack by the bromine atom is thus on the CF_2 group of the olefin:

$$Br{\cdot} + CF_2{:}CHCl \longrightarrow CF_2Br{\cdot}CHCl{\cdot} \xrightarrow{HBr} CF_2Br{\cdot}CH_2Cl + Br{\cdot}$$

[1] Haszeldine and Steele, *J.*, 1954, 923.
[2] *Idem*, *J.*, 1955, 3005.

The polarisation of the double bond in chloro-1 : 1-difluoroethylene during reactions involving ionic intermediates is shown to be $\overset{\delta+}{CF_2}:\overset{\delta-}{CHCl}$ by thermal reaction with hydrogen chloride to give 1 : 2-dichloro-1 : 1-difluoroethane (VII), an authentic sample of which was prepared by treatment of 1 : 1-difluoroethylene with chlorine. This polarisation is supported by the formation of 2-chloro-1 : 1 : 1-trifluoroethane (VIII) by reaction of the olefin with hydrogen fluoride,[3] by the base-catalysed addition of ethanol [4] to give 2-chloro-1 : 1-difluoroethyl ethyl ether :

$$EtO^- + CF_2{:}CHCl \longrightarrow EtO{\cdot}CF_2{\cdot}\dot{C}HCl^- \xrightarrow{EtOH} EtO{\cdot}CF_2{\cdot}CH_2Cl + EtO^-$$

and by the formation of 2-chloro-1 : 1-difluoro-1-iodoethane $CF_2I{\cdot}CH_2Cl$ on reaction with hydrogen iodide.[5]

The evidence summarised above thus shows that radical and atomic attack on chloro-1 : 1-difluoroethylene is predominantly, and probably exclusively, on the CF_2 group. This again [6] shows that a radical does not behave as an electrophilic reagent during its attack on unsaturated systems. The concept being adopted that intermediate radical stability determines the direction of radical addition to an olefin, it follows that the radical $\dot{C}F_3{\cdot}CF_2{\cdot}CHCl$ is more stable than $CF_3{\cdot}CHCl{\cdot}\dot{C}F_2$, *i.e.*, to a first approximation replacement of only one hydrogen of a CH_2 group by chlorine gives a radical more stable than one produced by replacement of both hydrogens in the CH_2 group by fluorine.

It was pointed out earlier [7] that radical stability decreases in the order tertiary > secondary > primary, where the terms tertiary, secondary, and primary indicate the number of atoms or groups other than hydrogen attached to the α-carbon atom and do not necessarily refer to the carbon skeleton. It was also noted [7] that, by suitable choice of stabilising groups or atoms R and R′ in a secondary radical RR′CH·, the stability of a secondary radical can in special cases by made greater than that of a tertiary radical which carries groups or atoms which have only a weak stabilising effect on the radical. The greater stability of the secondary radical $CF_3{\cdot}CF_2{\cdot}\dot{C}HCl$ (R = C_2F_5, R′ = Cl) compared with the tertiary radical $CF_3{\cdot}CHCl{\cdot}\dot{C}F_2$ thus exemplifies this overlap region between secondary and tertiary radicals. It is similarly clear that attack by a trifluoromethyl radical or bromine atom on an olefin such as $CF_3{\cdot}CF{:}CHCl$ will be on the CF group, since the secondary radical $CF_3{\cdot}CFR{\cdot}\dot{C}HCl$ will be more stable than the tertiary radical $CF_3{\cdot}\dot{C}F{\cdot}CHClR$ (R = perfluoroalkyl, Br, etc.).

The ease of radical attack on chloro-1 : 1-difluoroethylene is roughly comparable with that on chlorotrifluoroethylene.[8] The propagation step ($CF_3{\cdot}CF_2{\cdot}\dot{C}HCl + CF_2{:}CHCl \longrightarrow CF_3{\cdot}CF_2{\cdot}CHCl{\cdot}CF_2{\cdot}\dot{C}HCl$) occurs less readily than with chlorotrifluoroethylene, however, and it is thus comparatively easy to obtain the 1 : 1 adduct in good yield by use of an excess of the chain-transfer agent.

Park, Seffl, and Lacher [9] considered that the reaction of trifluoroiodoethylene with chloro-1 : 1-difluoroethylene gave 3-chloro-1 : 1 : 2 : 4 : 4-pentafluoro-4-iodobut-1-ene ($CF_2{:}CFI + CF_2{:}CHCl \longrightarrow CF_2{:}CF{\cdot}CHCl{\cdot}CF_2I$), thus intimating that radical attack takes place on a CHCl group before a CF_2 group. Since attack of both a trifluoromethyl radical and a bromine atom is actually on the CF_2 group of the olefin, it is extremely unlikely that the $CF_2{:}\dot{C}F{\cdot}$ radical would attack the CHCl group of the olefin. The product actually obtained by Park *et al.* is clearly 4-chloro-1 : 1 : 2 : 3 : 3-pentafluoro-4-iodobut-1-ene $CF_2{:}CF{\cdot}CF_2{\cdot}CHClI$.

[3] Henne and Arnold, *J. Amer. Chem. Soc.*, 1948, **70**, 758.
[4] B.P. 583,874; *Chem. Abs.*, 1947, **41**, 5142.
[5] Haszeldine and Osborne, *J.*, 1956, 61.
[6] Haszeldine and Steele, *J.*, 1953, 1199 *et seq.*
[7] Haszeldine, *J.*, 1953, 3565.
[8] Haszeldine and Steele, *J.*, 1953, 1592.
[9] Park, Seffl, and Lacher, *J. Amer. Chem. Soc.*, 1956, **78**, 59.

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Experimental

Preparation of Chloro-1 : 1-*difluoroethylene*.—The olefin, b. p. −18·0° (Found : *M*, 98·5. Calc. for C_2HClF_2 : *M*, 98·5), was prepared from 1 : 1-dichlorodifluoroethylene in 98% yield by photochemical reaction with hydrogen bromide followed by debromochlorination; its purity was checked by means of its infrared spectrum.

Reaction of Chloro-1 : 1-*difluoroethylene with Trifluoroiodomethane*.—(a) *In Pyrex vessels*. The olefin (3·08 g., 0·031 mole) and trifluoroiodomethane (12·6 g., 0·064 mole), sealed in a 600-ml. Pyrex tube, did not react in the dark during 14 days. The lower portion of the tube was then shielded and the vapour phase was exposed to ultraviolet light for 28 days to give unchanged reactants (14·4 g., 91%) and 3-*chloro*-1 : 1 : 1 : 2 : 2-*pentafluoro*-3-*iodopropane* (1·20 g., 94%), b. p. 102°, n_D^{20} 1·404 (Found : C, 12·5; H, 0·5. C_3HClF_5I requires C, 12·2; H, 0·3%).

(b) *In silica vessels*. In a typical small-scale experiment, the olefin (1·26 g., 0·013 mole) and trifluoroiodomethane (6·3 g., 0·032 mole) in a 200-ml. silica tube were similarly irradiated for 6 days to give unchanged trifluoroiodomethane (3·8 g., 60%), liquid products (3·44 g.), and a mixture (0·15 g.) of hexafluoroethane and chlorotrifluoromethane (analysed by infrared spectroscopy). Distillation of the liquid products gave 3-chloro-1 : 1 : 1 : 2 : 2-pentafluoro-3-iodopropane (2·7 g., 72%), b. p. 102°, shown by infrared spectroscopic examination to be identical with the material obtained as in (a) above, and a residue (0·6 g.) of $CF_3{\cdot}[CF_2{\cdot}CHCl]_2{\cdot}I$ (Found : C, 15·4; H, 0·5. $C_5H_2Cl_2F_7I$ requires C, 15·4; H, 0·5%). The conditions used in the above reaction were designed to prevent the propagation reaction as much as possible.

Reaction of 3-*Chloro*-1 : 1 : 1 : 2 : 2-*pentafluoro*-3-*iodopropane with Chlorine*.—In a typical experiment, the iodo-compound (2·40 g., 0·0081 mole) was mixed with chlorine (0·40 g., 0·0056 mole) in a 50-ml. Pyrex tube and exposed to ultraviolet light for 2 days. Mercury was then added and the liquid products were distilled *in vacuo*, to give unchanged iodo-compound (*ca.* 0·6 g.), and a fraction redistilled through a small column to give 3 : 3-*dichloro*-1 : 1 : 1 : 2 : 2-*pentafluoropropane* (1·00 g., 87%), b. p. 53°/771 mm., n_D^{20} 1·326 (Found : C, 17·4; H, 0·7%; *M*, 200. $C_3HCl_2F_5$ requires C, 17·7; H, 0·5%; *M*, 203). This compound shows strong infrared bands at 3·30, 7·42, 7·46, 8·10, 8·28, 8·74, 9·23, 9·60, 10·06, 11·91, 12·50, 13·18, 13·97, and 14·05 μ.

Synthesis of 3 : 3-*Dichloro*-1 : 1 : 1 : 2 : 2-*pentafluoropropane*.—Reaction of an excess of 3-chloro-1 : 1 : 1 : 2 : 2-pentafluoropropane (3·31 g.) with chlorine (0·75 g.) and water (2 ml.) in a 20-ml. Pyrex tube exposed to a Hanovia arc for 2 days gave 3 : 3-dichloro-1 : 1 : 1 : 2 : 2-pentafluoropropane (61%) (Found : *M*, 202), b. p. (isoteniscope) 50°/735 mm.; its infrared spectrum was identical with that of the compound prepared by reaction of the compound (I) with chlorine.

Synthesis of 3-*Chloro- and* 3-*Iodo*-1 : 1 : 1 : 2 : 2-*pentafluoropropane*.—The toluene-*p*-sulphonate of pentafluoropropanol [10] (7·7 g.), prepared in the conventional manner, was treated with a 100% excess of potassium chloride in refluxing diethylene glycol monobutyl ether for 4 hr. The volatile product, condensed in liquid oxygen, was transferred to an apparatus for manipulation of volatile compounds, and distilled to give 3-*chloro*-1 : 1 : 1 : 2 : 2-*pentafluoropropane* (71%) (Found : C, 21·4; H, 1·5%; *M*, 168. $C_3H_2ClF_5$ requires C, 21·4; H, 1·4%; *M*, 168·5), b. p. 28° (isoteniscope).

Reaction of the toluene-*p*-sulphonate (6·9 g.) with potassium iodide (100% excess) similarly yielded 3-iodo-1 : 1 : 1 : 2 : 2-pentafluoropropane (75%) (Found : *M*, 259. Calc. for $C_3H_2F_5I$: *M*, 260), b. p. 72°. The iodo-compound (2·7 g.), sealed *in vacuo* in a 10-ml. Pyrex tube containing chlorine (10% excess) and kept in the dark for 3 days, then exposed to ultraviolet light for 8 hr., gave a volatile product which when washed with cold dilute aqueous sodium hydroxide and distilled *in vacuo* was identified as 3-chloro-1 : 1 : 1 : 2 : 2-pentafluoropropane (77%) (Found : *M*, 169. Calc. for $C_3H_2ClF_5$: *M*, 168·5).

Tiers, Brown, and Reid [11] used lithium halides to convert the toluene-*p*-sulphonates of fluoro-alcohols into the corresponding halides, but reported that the sodium halides were ineffective; satisfactory yields can clearly be obtained by using potassium halides.

Reaction of 1 : 1 : 3 : 3 : 3-*Pentafluoropropene with Chlorine*.—The olefin (0·85 g.), prepared by dehydroiodination of 1 : 1 : 3 : 3 : 3-pentafluoro-1-iodopropane,[8] was sealed in a Pyrex tube with chlorine (0·48 g.) and exposed to daylight for 24 hr., then to ultraviolet light for 4 hr.

[10] Haszeldine and Leedham, *J.*, 1953, 1548.
[11] Tiers, Brown, and Reid, *J. Amer. Chem. Soc.*, 1953, **75**, 5978.

Mercury was added and the product was distilled to give 1 : 2-*dichloro*-1 : 1 : 3 : 3 : 3-*pentafluoropropane* (1·15 g., 90%), b. p. 51°, n_D^{20} 1·323 (Found : C, 17·2; Cl, 34·5%; *M*, 203. $C_3HCl_2F_5$ requires C, 17·7; Cl, 35·0%; *M*, 203). This compound shows strong infrared bands at 3·35, 7·45, 7·90, 8·25, 8·65, 8·87, 9·55, 10·10, 11·10, 12·13, 12·29, 14·07, 14·16, 14·55, and 14·85 μ.

Action of Zinc and Ethanol on 3-*Chloro*-1 : 1 : 1 : 2 : 2-*pentafluoro*-3-*iodopropane*.—The iodo-compound (4·12 g.) was slowly added to a well-stirred mixture of zinc dust (15 g.) and refluxing ethanol (30 ml.). After 5 hr. the volatile products which had been formed were carried through the water-condenser by a stream of dry nitrogen and collected in a trap cooled to −183°. Distillation *in vacuo* gave a fraction shown by infrared spectroscopy to be free from 1 : 1 : 3 : 3 : 3-pentafluoropropene. 3-Chloro-1 : 1 : 1 : 2 : 2-pentafluoropropane (40%) and 2 : 3 : 3 : 3-tetrafluoropropene (30%) were identified as the main products by spectroscopy. The olefin was removed by reaction with chlorine in the dark, and the dichloride, after separation from the monochloro-compound by distillation, was treated with zinc and ethanol to regenerate the olefin. Further spectroscopic examination then confirmed the original analysis.

3-Chloro-1 : 1 : 1 : 2 : 2-pentafluoropropane was shown to react with zinc and ethanol in a sealed tube at 70° to give 2 : 3 : 3 : 3-tetrafluoropropene (53%). 1 : 1 : 1 : 2 : 2-Pentafluoro-3-iodopropane similarly gave the olefin in 87% yield.

Reaction of Chloro-1 : 1-*difluoroethylene with Hydrogen Bromide*.—The olefin (0·75 g., 0·0076 mole) and hydrogen bromide (0·615 g., 0·0076 mole) were sealed in a 100-ml. Pyrex tube and kept in the dark for 6 weeks; no reaction occurred. When the olefin (3·20 g., 0·0325 mole) and hydrogen bromide (2·66 g., 0·0328 mole) were sealed in a 200-ml. silica tube, and the vapour phase was exposed to ultraviolet light, immediate reaction was seen and after 6 hr. distillation gave 1-*bromo*-2-*chloro*-1 : 1-*difluoroethane* (5·80 g., 99%), b. p. 70·2°/776 mm., n_D^{20} 1·404 (Found : C, 13·4; H, 1·3. $C_2H_2BrClF_2$ requires C, 13·4; H, 1·1%).

The bromo-compound (3·51 g.), dissolved in ethanol (5 ml.), was slowly added to a stirred mixture of zinc dust (10 g.) and refluxing ethanol (10 ml.) and after a further 2 hr. the volatile products were swept from the apparatus by a stream of nitrogen. Distillation *in vacuo* gave 1 : 1-difluoroethylene (1·20 g., 95%) (Found : *M*, 63·5. Calc. for $C_2H_2F_2$: *M*, 64), identified by its infrared spectrum.

Reaction of Chloro-1 : 1-*difluoroethylene with Hydrogen Chloride*.—The olefin (1·08 g., 0·11 mole) and hydrogen chloride (0·72 g., 0·02 mole), sealed in a 150-ml. Pyrex tube, did not react at 250° for 2 days. Reaction occurred at 270° and after 2 days distillation gave hydrogen chloride (0·368 g.) and 1 : 2-dichloro-1 : 1-difluoroethane (1·40 g., 91%), b. p. 47°, identified by its infrared spectrum.

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421. *Some New Benziminazole Derivatives.*

By P. R. THOMAS and G. J. TYLER.

A synthesis of benziminazoles from imidoate hydrochlorides and *o*-phenylenediamines described by King and Acheson [1] is of particular value for the preparation of 2-arylbenziminazoles. For 2-alkyl derivatives it is not so useful when the *o*-diamine possesses an electrophilic substituent in the 4-position.

KING and ACHESON [1] have prepared numerous 2-alkylbenziminazoles by reaction of *o*-phenylenediamines with alkyl imidoate hydrochlorides in methanol. This method has now been applied to the synthesis of some 2-arylbenziminazoles, in preference to others [2] because, in general, it gave higher yields of purer products. Weidenhagen's method [3]

[1] King and Acheson, *J.*, 1949, 1396.
[2] Partridge and Turner, *J. Pharm. Pharmacol.*, 1953, **5**, 114; Hölljes and Wagner, *J. Org. Chem.*, 1944, **9**, 43; Porai-Koshits *et al.*, *J. Gen. Chem. U.S.S.R.*, 1947, **17**, 1768; 1949, **19**, 1545.
[3] Weidenhagen, *Ber.*, 1936, **69**, 2263; 1942, **75**, 1936.

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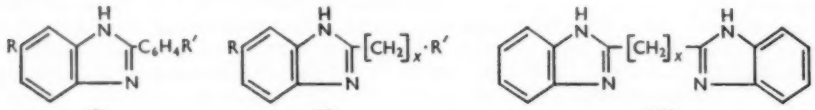
whereby *o*-phenylenediamines and aromatic aldehydes are condensed in the presence of cuprous acetate uses relatively inaccessible aldehydes and gives lower yields. We thus prepared the benziminazoles (I) in which R = R′ = H (83%), Me (81%), and CO_2Me (92%) and the bisiminazoles (III; $x = 4$ and 8).[4]



(I) (II) (III)

Where the *o*-diamine carried an electrophilic substituent, *e.g.*, 4-NO_2 or 4-CO_2Me, it reacted with difficulty and gave a low yield of benziminazole. By this method small quantities of 2-(ω-carboxy-*n*-octyl)-5-methoxycarbonylbenziminazole (II; R = CO_2Me, R′ = CO_2H, $x = 8$) and 2-(ω-carboxy-*n*-octyl)-5-nitrobenziminazole (II; R = NO_2, R′ = CO_2H, $x = 8$) were obtained but such derivatives were better prepared by condensing the *o*-phenylenediamine derivative with excess of the carboxylic acid in 4N-hydrochloric acid.[5]

Attempts to prepare 5-carboxy-2-*p*-carboxyphenylbenziminazole by oxidation of 5-methyl-2-*p*-tolylbenziminazole with alkaline permanganate or chromic acid gave low yields of an impure product. The corresponding dimethyl ester, however, was obtained in high yield by the imidoate method, and alkaline hydrolysis gave the very high-melting, insoluble diacid, which was characterised as its salts with hexamethylene- and decamethylene-diamine.

Of the intermediates, ethyl *p*-methoxycarbonylbenzimidoate hydrochloride was prepared from methyl *p*-cyanobenzoate by Pinner's method.[6] Methyl 3 : 4-diaminobenzoate was prepared from aceto-*p*-toluidide in five stages in an overall yield of about 40%; nitration [7] gave 4-acetamido-3-nitrotoluene which was oxidised in neutral permanganate [8] to 4-acetamido-3-nitrobenzoic acid; hydrolysis then gave the amino-acid which was esterified and hydrogenated to methyl 3 : 4-diaminobenzoate.

2-(ω-Carboxy-*n*-octyl)-5-nitrobenziminazole was prepared as its hydrate by the condensation of 4-nitro-*o*-phenylenediamine with a large excess of sebacic acid in 4N-hydrochloric acid solution. The benziminazole derivative was converted into its methyl ester, which on hydrogenation gave 5-amino-2-(ω-methoxycarbonyl-*n*-octyl)benziminazole (II; R = NH_2, R′ = CO_2Me, $x = 8$). After reaction of methyl 3 : 4-diaminobenzoate and excess of sebacic acid 5-carboxy-2-(ω-carboxy-*n*-octyl)benziminazole (II; R = R′ = CO_2H, $x = 8$) was obtained *via* its hydrochloride.

Experimental

Amine Equivalent.—The equivalents of benziminazole derivatives were determined in acetic acid by titration with perchloric acid in acetic acid, α-naphtholbenzein being used as indicator.

Ethyl Benzimidoate Hydrochlorides.—Hydrogen chloride was passed into a mixture of nitrile, absolute ethanol and, sometimes, benzene at 0—5° until at least the theoretical quantity had been absorbed. After 1—3 days the product had solidified and was filtered off, washed with ether, and dried. Details are in Table 1.

Benziminazoles prepared from Ethyl Imidoate Hydrochlorides.—Approx. equimolecular quantities of imidoate hydrochloride and aromatic *o*-diamine in methanol were heated under reflux for 1 hr., then cooled, and filtered, and the filtrate was evaporated to small bulk and poured into water. The product was filtered off and recrystallised.

[4] Cf. Shriner and Upson, *J. Amer. Chem. Soc.*, 1941, **63**, 2277.
[5] Phillips, *J.*, 1928, 2395, 3131.
[6] Pinner, "Die Imidoaether und ihre Derivate," Verlag R. Oppenheimer, Berlin, 1892.
[7] Gattermann, *Ber.*, 1885, **18**, 1483.
[8] Ullmann and Mauthner, *Ber.*, 1903, **36**, 4032.

The reaction mixture containing 2-(ω-carboxy-*n*-octyl)-5-nitrobenziminazole was poured into sodium hydroxide solution, the insoluble unchanged diamine filtered off, and the filtrate acidified to give the crude product.

Details of conditions and *products* are in Table 2.

TABLE 1. *Preparation of ethyl imidoate hydrochlorides.*

Nitrile (g.)	EtOH (c.c.)	C_6H_6 (c.c.)	Product Formula [X = ·C(OEt):NH$_2$Cl]	Yield (%)
250	150	—	PhX	90
30	16	—	*p*-C_6H_4MeX	90
132	42	400	*p*-CO_2Me·C_6H_4X	82
36·6	13	215	$HO_2C·[CH_2]_6·X$ *	52
54	70	300	$X·[CH_2]_4·X$	64
37·6	26	200	$X·[CH_2]_8·X$	68

* Solidified only when washed; slightly impure.

TABLE 2. *Some benziminazoles prepared from imidoate salts.*

No.	Diamine (g.)	Imidoate, HCl (g.)	MeOH (c.c.)	Product	Yield (%)	M. p.	Solvent for crystn.
1	180	280	1000	I; R = R′ = H	85	295°	MeOH
2	22·7 [b]	42	115	I; R = R′ = Me *	81	195	C_6H_6
3	25	38·6	500	I; R = R′ = CO_2Me	92	237	Dioxan
4	10·5	16·9	100	II; R = CO_2Me, R′ = CO_2H; *x* = 8 [c]	23	142—144	Aq. MeOH
5	5·6	9·84	50	II; R = NO_2, R′ = CO_2H; *x* = 8 [d]	19	104—107	Aq. $COMe_2$
6	5·0	6·3	40	III; *x* = 4	52	259	Aq. EtOH
7	21·6	32·9	150	III; *x* = 8	50	270	,,

No.	Found (%) C	H	N	OMe	Found Amine equiv.	Formula	Required (%) C	H	N	OMe	Reqd. Amine equiv.
2	80·7	6·4	12·8	—	223	$C_{13}H_{14}N_2$	81·1	6·3	12·7	—	222
3	66·1	4·7	9·3	19·5	311	$C_{17}H_{14}O_4N_2$	65·8	4·5	9·1	19·9	310
4	64·8	7·0	8·9	10·1	333	$C_{18}H_{24}O_4N_2$	65·1	7·2	8·4	9·3	332
5	56·7	6·8	12·8	—	340	$C_{16}H_{21}O_4N_3,H_2O$	57·0	6·8	12·5	—	337
7	76·4	8·1	15·8	—	—	$C_{22}H_{26}N_4$	76·3	7·5	16·2	—	—

Footnotes to Table 2: (*a*) The *picrate* crystallised from alcohol as pale needles, m. p. 278—280° (decomp.) (Found: C, 56·2; H, 3·8; N, 15·0. $C_{21}H_{17}O_7N_5$ requires C, 55·9; H, 3·8; N, 15·5%). The *hydrochloride*, prepared by passing dry hydrogen chloride through a hot benzene solution of the base, had m. p. 290° (decomp.), and was easily hydrolysed by boiling water (Found: Cl, 13·8. $C_{15}H_{15}N_2Cl$ requires Cl, 13·7%).

This benziminazole was prepared by two further routes. (i) 3 : 4-Diaminotoluene (54 g.) and *p*-toluic acid (59·6 g.) were heated for 2 hr. at 180°, then boiled with 10% hydrochloric acid (500 c.c.) to remove unchanged diamine, and the insoluble product filtered off and boiled with 5% sodium hydroxide solution to remove unchanged acid. The residual solid was washed with water, dried and crystallised (charcoal) from benzene, giving 5-methyl-2-*p*-tolylbenziminazole as a grey solid (50% yield), m. p. 192—194°. (ii) 3 : 4-Diaminotoluene dihydrochloride (40 g.) and *p*-toluonitrile (22 g.) were heated at 180° for 3 hr. The product was extracted continuously with ether for 4 hr., dried, and boiled with 5% sodium hydroxide solution (250 c.c.). The product was filtered off, washed with water, and dried and then crystallised as before (50—60%; m. p. 193—194°).

(*b*) Distillation of the diamine followed by crystallisation from benzene–light petroleum gave an almost white product, m. p. 88—90°.

(*c*) The corresponding dicarboxylic acid was isolated thus. The oily product obtained from methyl 3 : 4-diaminobenzoate (50 g.) and ethyl ω-carboxynonanimidoate hydrochloride (85·9 g.) was extracted several times with ether to remove unchanged diamine. The residual oil was then hydrolysed with boiling 10% sodium hydroxide solution (500 c.c.) for 5 hr.

Neutralisation of the solution with acetic acid precipitated the crude *benziminazoledicarboxylic acid*. This was recrystallised twice from aqueous acetic acid and dried *in vacuo* at 80° for 16 hr. to decompose the unstable acetate, giving 5-carboxy-2-(ω-carboxy-*n*-octyl)benziminazole (31 g.), m. p. 223—225°.

(*d*) Isolated as monohydrate. The *methyl ester* was obtained (as straw-coloured needles, m. p. 124—125°) by esterification of 2-(ω-carboxy-*n*-octyl)-5-nitrobenziminazole with 5% methanolic hydrogen chloride (Found : C, 60·6; H, 6·7; N, 12·2; OMe, 9·1%; amine equiv., 335. $C_{17}H_{23}O_4N_3$ requires C, 61·2; H, 6·9; N, 12·6; OMe, 9·3%; amine equiv., 333) : it did not form a hydrochloride.

2-p-*Carboxyphenylbenziminazole-5-carboxylic Acid* (I; R = R′ = CO_2H).—Methyl 2-(*p*-methoxycarbonylphenyl)benziminazole-5-carboxylate (18 g.) was boiled under reflux for 3 hr. with sodium hydroxide (4 g.) in ethanol (250 c.c.), then evaporated to dryness, and the residue was dissolved in water (100 c.c.). After filtration the solution was acidified with acetic acid. The solid *acid* was filtered off, washed with water, and dried (yield quantitative); it did not melt below 350° (Found : C, 64·0; H, 3·6; N, 10·0%; amine equiv., 279. $C_{15}H_{10}O_4N_2$ requires C, 63·8; H, 3·6; N, 9·9%; amine equiv., 282).

The acid (5 g.) was dissolved with warming in an aqueous solution (100 c.c.) of hexamethylenediamine (2·2 g.). After filtration, the solution was concentrated to 25 c.c. and cooled. The *salt* was filtered off, washed with methanol, and dried (5·2 g., 73%); it had m. p. 260—262° (Found : amine equiv., 135. $C_{21}H_{30}O_4N_4$ requires amine equiv., 133).

The *decamethylenediammonium salt* (70% yield), similarly obtained, melted at 213—216° (Found : amine equiv., 150. $C_{25}H_{34}O_4N_4$ requires amine equiv., 151).

5-*Amino*-2-(ω-*carboxy*-n-*octyl*)*benziminazole* (II; R = NH_2, R′ = CO_2H, *x* = 8).—2-(ω-Carboxy-*n*-octyl)-5-nitrobenziminazole (57 g.) was dissolved in boiling aqueous sodium hydroxide (37·5 g. in 400 c.c.). Sodium dithionite (hydrosulphite) (72 g.) was added in three portions. When the vigorous reaction had subsided, a solution of sodium hydroxide (30 g.) in water (120 c.c.) and sodium dithionite (72 g.) were added consecutively and the solution was boiled until almost colourless, then diluted to 1 l.; the *amino-acid*, precipitated by addition of hydrochloric acid, crystallised (charcoal) from aqueous ethanol (yield, 30 g.) (Found : amine equiv., 159. $C_{16}H_{23}O_2N_3,2H_2O$ requires amine equiv., 162·5). The hydrate was dried overnight at 50° *in vacuo*, giving the anhydrous *compound*, m. p. 140—143° (Found : amine equiv., 146. $C_{16}H_{23}O_2N_3$ requires amine equiv., 144·5).

5-*Amino*-2-(ω-*methoxycarbonyl*-n-*octyl*)*benziminazole* (II; R = NH_2, R′ = CO_2Me, *x* = 8).—(*a*) The foregoing acid dihydrate (21·7 g.) was boiled under reflux in 6% methanolic hydrogen chloride (250 c.c.) for 4 hr., then concentrated; the *ester dihydrochloride* crystallised; it was recrystallised from methanol (Found : C, 53·8; H, 6·5; N, 11·2; OMe, 8·0; Cl, 18·8. $C_{17}H_{27}O_2N_3Cl_2$ requires C, 54·2; H, 6·6; N, 11·1; OMe, 8·2; Cl, 18·9%). The free *ester*, obtained by treatment with warm sodium carbonate solution, recrystallised from benzene as pale pink plates (17·9 g.), m. p. 97—98° (Found : C, 66·9; H, 8·3; N, 13·9; OMe, 10·2%; amine equiv., 154. $C_{17}H_{25}O_2N_3$ requires C, 67·3; H, 8·2; N, 13 8; OMe, 10·2%; amine equiv., 152).

(*b*) 2-(ω-Methoxycarbonyl-*n*-octyl)-5-nitrobenziminazole (10 g.) was hydrogenated in ethyl acetate (200 c.c.) in the presence of 10% platinum–carbon (2 g.) at atmospheric pressure. When the theoretical quantity of hydrogen had been absorbed, the catalyst was filtered off and the filtrate evaporated to dryness. The residue on recrystallisation from benzene gave the 5-amine (8 g.), m. p. 97—98°.

The Phillips [5] procedure was employed for the synthesis of other benziminazolecarboxylic acids or their derivatives.

2-(ω-*Carboxy*-n-*octyl*)-5-*nitrobenziminazole* (II; R = NO_2, R′ = CO_2H, *x* = 8).—4-Nitro-*o*-phenylenediamine (100 g.) and sebacic acid (536 g.) were boiled under reflux in 4N-hydrochloric acid (3 l.) for 24 hr., then cooled, and the precipitate was filtered off, washed with water, and dried. Excess of sebacic acid was removed by continuous extraction with ether. The crude product was crystallised twice from aqueous acetone, yielding the monohydrate of 2-(ω-carboxy-*n*-octyl)-5-nitrobenziminazole as a pale yellow solid (78 g.), m. p. 105—108°.

5-*Carboxy*-2-(ω-*carboxy*-n-*octyl*)*benziminazole* (II; R = R′ = CO_2H, *x* = 8).—Methyl 3 : 4-diaminobenzoate (50 g.) and sebacic acid (240 g.) were boiled under reflux in 4N-hydrochloric acid (1500 c.c.) for 20 hr., then cooled and the precipitate was filtered off and then dried.

Continuous extraction with ether removed the excess of sebacic acid, leaving the hydrochloride of 5-carboxy-2-(ω-carboxy-*n*-octyl)benziminazole. This was dissolved in sodium hydroxide solution and the crude dicarboxylic acid precipitated by acetic acid. It was filtered off, recrystallised twice from aqueous acetic acid, and dried for 16 hr. at 80° *in vacuo*. The dicarboxylic acid (36 g.) had m. p. 223—225° (Found: C, 63·8; H, 7·0; N, 8·8%; amine equiv., 325. $C_{17}H_{22}O_4N_2$ requires C, 64·1; H, 6·9; N, 8·8%; amine equiv., 318).

2-(ω-*Methoxycarbonyl*-n-*butyl*)*benziminazole* (II; R = H, R′ = CO_2Me, $x = 4$).—*o*-Phenylenediamine (16·2 g.) and adipic acid (87·6 g.) were boiled under reflux in 4N-hydrochloric acid (200 c.c.) for 21 hr. The solid which was deposited from the cooled solution was filtered off and esterified under reflux for 8 hr. with 3% methanolic hydrogen chloride (200 c.c.). The solution was evaporated to small bulk, then water (500 c.c.) was added. Dimethyl adipate separated as an oil which was removed by repeated extraction with ether. The aqueous solution was neutralised with sodium carbonate, and the *benziminazole* was precipitated, filtered off, and recrystallised from water as white needles (16·1 g.), m. p. 141° (Found: N, 12·2%; amine equiv., 229. $C_{13}H_{16}O_2N_2$ requires N, 12·1%; amine equiv., 232).

2-(ω-*Carboxy*-n-*octyl*)*benziminazole* (II; R = H, R′ = CO_2H, $x = 8$).—*o*-Phenylenediamine (10·8 g.) and sebacic acid (40·4 g.) were heated under reflux in 4N-hydrochloric acid for 4 hr., then cooled and the precipitate was filtered off, washed with water, and dried. Excess of sebacic acid was removed by continuous extraction with ether and the residue crystallised from water. 2-(ω-*Carboxy*-n-*octyl*)*benziminazole hydrochloride* was obtained as white needles (8·5 g.), m. p. 168—170° (Found: Cl, 11·3. $C_{16}H_{23}O_2N_2Cl$ requires Cl, 11·4%). A solution of the hydrochloride (3·1 g.) in warm water (300 ml.) was carefully neutralised with sodium hydroxide solution. The *benziminazolecarboxylic acid* was filtered off and crystallised twice from aqueous ethanol as white needles (2·4 g.), m. p. 117—118° (Found: N, 10·1%; acid equiv., 272; amine equiv., 276·5. $C_{16}H_{22}O_2N_2$ requires N, 10·2%; acid equiv., 274; amine equiv., 274).

4-*Acetamido*-3-*nitrobenzoic Acid*.—4-Acetamido-3-nitrotoluene [7] (400 g.) and magnesium sulphate (400 g.) in water (750 c.c.) were heated to the b. p. An aqueous solution of potassium permanganate (1 kg.) was added during 4 hr. The manganese dioxide was filtered off and the filtrate and washings were concentrated and cooled, unchanged 4-acetamido-3-nitrotoluene (35 g.) being recovered. Acidification of the concentrated solution with hydrochloric acid gave 4-acetamido-3-nitrobenzoic acid (276 g., 67%), m. p. 285—286°.

4-*Amino*-3-*nitrobenzoic Acid*.—4-Acetamido-3-nitrobenzoic acid was boiled under reflux with 5% hydrochloric acid for 1 hr. The solution was cooled and an almost quantitative yield of product, m. p. 284—288°, was filtered off.

This acid with methanol and sulphuric acid gave the methyl ester (95%), m. p. 196—198°.

Methyl 3 : 4-*Diaminobenzoate*.—Methyl 4-amino-3-nitrobenzoate (20 g.) was hydrogenated in ethyl acetate (250 c.c.) and 10% platinum–charcoal (1 g.) at atmospheric pressure until the theoretical quantity of hydrogen had been absorbed. The catalyst was removed; the filtrate was dried ($CaCl_2$) and evaporated. The yield of product, m. p. 108—109°, was quantitative.

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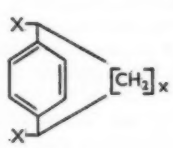
422. *The Preparation of Some* para-*Bridged Benzene Derivatives.*

By K. Jasper Clark.

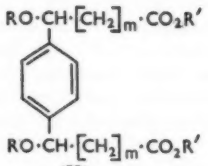
p-Tetradecamethylenebenzene has been prepared by the intramolecular condensation of *p*-di-(6-methoxycarbonylhexyl)benzene, and reduction of the resultant acyloin. Dibromination of the hydrocarbon, on the αα′-carbon atoms, was effected with *N*-bromosuccinimide, and the product converted into the αα′-diethoxy-derivative. An oxindolyl derivative of *p*-tridecamethylenebenzene is probably produced on interaction of *p*-(7-hydroxy-8-oxotetradecamethylene)benzene with phenylhydrazine. Attempts to cyclise *p*-di-(3-oxo-6-methoxycarbonylhexyl)benzene, and to prepare the *p*-nonamethylenebenzene system, failed.

It was desired to prepare compounds of type (I) with the immediate object of replacing the groups X by a second, linking alkylene chain and the ultimate object of preparing "interlocking" molecules.[1] From Catalan models it appeared that the encircling *cyclo*-alkane ring must contain at least 18 methylene groups.

Attempts to prepare dihydroxy-acids (II; R = H), where $m > 2$, or their diketo-analogues, for acyloin condensation and reduction, failed. The products from terephthaloyl dichloride and substituted malonic acids [2] gave poor results on hydrolysis; and the products from diethyl disodioterephthaloyldiacetate and aliphatic ω-halogeno-esters gave mainly terephthalic acid on hydrolysis.



(I)



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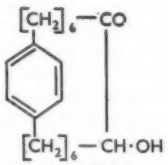

(III)

Acyloin condensations of *p*-di-(ω-alkoxycarbonylalkyl)benzenes and subsequent reduction have recently given good yields of *p*-decamethylene-[3] and *p*-dodecamethylene-benzene,[4] and such compounds might be reactive at the α-positions. Three parallel cases have now been investigated.

Condensation of *p*-xylylene dibromide and dihydroresorcinol, and hydrolysis of the product, gave *p*-di-(6-carboxy-3-oxohexyl)benzene, but the derived dimethyl ester gave polymers on attempted acyloin condensation, probably because of reaction of the $CO{\cdot}CH_2$ groups with the sodium used as condensing agent. However, Wolff–Kishner reduction of the diketo-acid gave *p*-di-(6-carboxyhexyl)benzene, and the derived ester was cyclised in good yield to the acyloin (III). This had the expected infrared absorption bands at 5·86 (CO) and 2·84 μ (OH) in Nujol mull, although it did not react with acetic anhydride, benzoyl chloride, aniline, or *o*-phenylenediamine, and with hydrazine gave a red oil. Clemmensen reduction then gave *p*-tetradecamethylenebenzene (I; x = 12, X = H), which with molecular bromine gave a gum but with *N*-bromosuccinimide gave a crystalline dibromo-derivative. The bromine atoms are labile towards sodium ethoxide, alcoholic potassium hydroxide, and pyridine, indicating their attachment to the aliphatic chain; and since *N*-bromosuccinimide normally attacks the α-position of aralkyl compounds, the

[1] Cf. Clark, *J.*, 1956 1511; 1957, 463.
[2] Parkes and Clark, *J.*, 1955, 3294.
[3] Wiesner, MacDonald, Ingraham, and Kelly, *Canad. J. Res.*, 1950, **28**, *B*, 561.
[4] Cram, Allinger, and Steinberg, *J. Amer. Chem. Soc.*, 1954, **76**, 6132.

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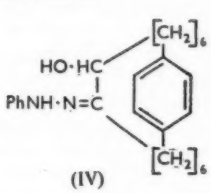
dibromo-derivative probably has structure (I; x = 12, X = Br). However, the dibromo-compound failed to react with sodiomalonic ester or potassium cyanide, and with potassium acetate in acetic acid gave only an impure acetoxy-derivative.

The acyloin (III) with phenylhydrazine in boiling aqueous acetic acid gave a chemically nert compound, $C_{26}H_{33}ON$, formally derived from 1 mol. of each reactant by loss of NH_4OH. This product has infrared absorption bands at 6·1 (CO·NH) and 3·01 μ (NH), and ultraviolet absorption maxima at 3150 (ε 10,400) and 2350 Å (ε 7000). It is suggested that this compound is the spiran (VI), that the phenylhydrazone (IV) first formed undergoes a Fischer reaction, giving the indole (V), which suffers Wagner–Meerwein rearrangement.



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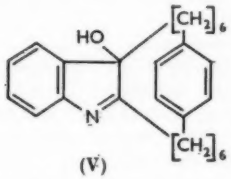

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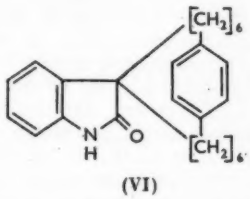

(VI)

In a third reaction series, Friedel–Crafts reaction of δ-ethoxycarbonylvaleroyl chloride and ethyl β-phenylpropionate and Wolff–Kishner reduction of the product gave 6-(*p*-2′-carboxyethylphenyl)hexanoic acid: the orientation of this was proved by oxidation of its methyl ester to terephthalic acid, but this ester was recovered unchanged after attempted acyloin condensation.

Experimental

p-*Di*-(2 : 6-*dioxo*cyclo*hexylmethyl*)*benzene*.—Stetter and Dierich's method [5] was modified as follows. Dihydroresorcinol (153 g.) and *p*-xylylene dibromide (90 g.) were stirred with a solution of potassium hydroxide (38 g.) in water (153 ml.) and ethanol (30 ml.) for 6 hr. on a boiling-water bath, then ethanol (1 l.) was added, and the mixture filtered hot at the pump. Washing with boiling ethanol gave a solid (70 g., 63%), insoluble in almost all organic solvents tried, but crystallising from dimethylformamide (Found: C, 73·3; H, 6·6. Calc. for $C_{20}H_{22}O_4$: C, 73·6; H, 6·7%); the crude solid charred at 150° and was pure enough for further reaction.

p-*Di*-(6-*carboxy*-3-*oxohexyl*)*benzene*.—*p*-Di-(2 : 6-dioxo*cyclo*hexylmethyl)benzene (43·75 g.) was refluxed with 10% sodium hydroxide solution (450 ml.) for 30 hr., then diluted with water (450 ml.) and acidified to Congo-red with concentrated hydrochloric acid. The precipitated acid, crystallised from a large volume of water, had m. p. 157° (38·85 g., 80%). The *diethyl*, m. p. 49·5—50·5° (from light petroleum, b. p. 60—80°) (Found: C, 68·7; H, 8·4. $C_{24}H_{34}O_6$ requires C, 68·9; H, 8·1%), and *dimethyl ester*, m. p. 72·5° (from methanol) (Found: C, 67·0; H, 8·0. $C_{22}H_{30}O_6$ requires C, 66·7; H, 7·9%), were prepared by use of sulphuric acid as catalyst.

Adding the dimethyl ester (10 g.) in xylene (300 ml.) during 30 hr. to sodium dust (11 g.) in xylene (1·5 l.), at 115° in nitrogen, gave unchanged ester (1·1 g.) and insoluble polymer (8·4 g.).

p-*Di*-(6-*carboxyhexyl*)*benzene*.—It was not possible to prepare this acid by combined hydrolysis and reduction of *p*-di-(2 : 6-dioxo*cyclo*hexylmethyl)benzene.[5] *p*-Di-(6-carboxy-3-oxohexyl)benzene (111 g.), 100% hydrazine hydrate (90 ml.), and potassium hydroxide (120 g.) were heated in ethylene glycol (1 l.) on the water-bath for 2 hr., then slowly to the b. p. while water and excess of hydrazine distilled off. After 14 hours' refluxing, cooling, and dilution with water (2 l.), acidification with concentrated hydrochloric acid to Congo-red gave crystals, m. p. 155—156° (from ethanol) (75 g., 73%). The *diethyl*, m. p. 24°, b. p. 230—240°/0·1 mm. (Found: C, 73·7; H, 9·7. $C_{24}H_{38}O_4$ requires C, 73·8; H, 9·7%), and *dimethyl ester*, m. p. 36·5°, b. p. 220°/0·14 mm. (Found: C, 72·9; H, 9·3. $C_{22}H_{34}O_4$ requires C, 72·9; H, 9·4%), were obtained as above.

p-(7-*Hydroxy*-8-*oxotetradecamethylene*)*benzene*.—The apparatus was essentially that described

[5] Stetter and Dierichs, *Chem. Ber.*, 1953, **86**, 693.

by Prelog *et al.*[6] I am indebted to Dr. R. B. Kelly[3] for further working details. The apparatus was dried for 24 hr. before use. From a mixture of sodium (11 g.) and sulphur-free xylene (1·5 l.; distilled from sodium), approx. 100 ml. of xylene were distilled; very fast stirring created a fine dust or emulsion of sodium in the boiling xylene. At 115—120°, with rapid stirring and under nitrogen, *p*-di-(6-methoxycarbonylhexyl)benzene (43·7 g.) was injected during 15—24 hr. The mixture was finally stirred for 2 hr. in nitrogen at 115°, then cooled to 0°. The temperature was kept below 30° while methanol (200 ml.) and then 20% sulphuric acid (300 ml.) were added. The xylene layer was washed with water (2 × 100 ml.), 10% sodium carbonate solution (2 × 200 ml.), and water (200 ml.), and dried (Na_2SO_4). On distillation in nitrogen yellow crystals of p-(7-*hydroxy*-8-*oxotetradecamethylene*)*benzene* (28·2 g., 79%) remained, smelling of musk. Distillation at 165—168°/0·1 mm. gave 25·55 g. (70%) of a light yellow solid which on further distillation had m. p. 67·8° (Found: C, 79·5; H, 10·1. $C_{20}H_{30}O_2$ requires C, 79·5; H, 9·9%).

p-*Tridecamethylenebenzene*-7′-spiro-3-*oxindole* (VI).—*p*-(7-Hydroxy-8-oxotetradecamethylene)benzene (1 g.) was refluxed with water (8 ml.), phenylhydrazine (5 ml.), and acetic acid (25 ml.) for 24 hr. The organic layer solidified. Pouring the whole into water gave the *spiran* (0·45 g.), m. p. 198° (from acetic acid) (Found: C, 83·3; H, 8·7; N, 3·6. $C_{26}H_{33}ON$ requires C, 83·2; H, 8·8; N, 3·7%). This product was inactive towards alcoholic potassium hydroxide, acetic anhydride, bromine in acetic acid, concentrated hydrochloric acid, and lithium aluminium hydride in ether. In concentrated sulphuric acid it gave a red solution.

p-*Tetradecamethylenebenzene*.—Amalgamated zinc wool (32 g.) and *p*-(7-hydroxy-8-oxotetradecamethylene)benzene (18 g.) in acetic acid (32 ml.) were refluxed for 24 hr., concentrated hydrochloric acid (5 × 32 ml.) being added at intervals during the first 12 hr. Dilution with water, extraction with ether, and washing with 10% sodium carbonate solution and water, drying (Na_2SO_4), evaporation, and distillation gave p-*tetradecamethylenebenzene*, (14·6 g., 90%), b. p. 120—125°/0·035—0·07 mm. (Found: C, 88·3; H, 11·8. $C_{20}H_{32}$ requires C, 88·2; H, 11·8%).

p-(1 : 14-*Dibromotetradecamethylene*)*benzene*.—*p*-Tetradecamethylenebenzene (8·4 g.) and *N*-bromosuccinimide (11 g.) with benzoyl peroxide (0·05 g.) in carbon tetrachloride (200 ml.) reacted vigorously at 100°. After refluxing for 1 hr. the mixture was filtered hot, then evaporated *in vacuo*, and the residual solid crystallised from acetone to yield p-(1 : 14-*dibromotetradecamethylene*)*benzene*, m. p. 163° (8 g.). More material (1·7 g.) was isolated by concentration of the mother-liquor. The dibromo-compound crystallised from acetone (Found: C, 56·0; H, 7·0; Br, 37·1. $C_{20}H_{30}Br_2$ requires C, 55·8; H, 7·0; Br, 37·2%). Crystallisation from alcohol lowered the yield because of formation of the ethoxy-compound.

Potassium acetate in glacial acetic acid gave an oil which could be distilled but did not give a good analysis for diacetoxy-compound despite indication of the presence of acetoxy-groups in the infrared spectrum.

p-(1 : 14-*Diethoxytetradecamethylene*)*benzene*.—To sodium (0·63 g.) in absolute alcohol (35 ml.) was added the preceding dibromo-compound (5·9 g.) in one portion. The solution was refluxed for 2 hr., cooled, and poured into dilute hydrochloric acid. The product was extracted with ether, washed with sodium carbonate solution, dried, and recovered. The *diethoxy-compound* distilled at 170°/0·03 mm. (Found: C, 80·3; H, 10·9. $C_{24}H_{40}O_2$ requires C, 80·0; H, 11·1%).

6-(p-2′-*Carboxyethylphenyl*)-2-*oxohexanoic Acid*.—Ethyl β-phenylpropionate (101 g.) was stirred with δ-ethoxycarbonylvaleryl chloride (135·5 g.) in carbon disulphide (1·2 l.). The solution was cooled to −10°, and anhydrous aluminium chloride (280 g.) added during 1 hr. After 5 hours' stirring at 0° and 18 hours' refluxing, ice and dilute hydrochloric acid were added and the organic layer separated and, with ethereal extracts of the aqueous layer, washed with water and dried (Na_2SO_4). The oil remaining on removal of the solvent was refluxed with 10% alcoholic potassium hydroxide (1·4 l.) for 3 hr. The alcohol was removed, water (1 l.) added, and the solution acidified to Congo-red with concentrated hydrochloric acid at <10°. After 1 hr. at <10° the precipitated *acid* was filtered off, washed with a little water, and crystallised from hot water (yield, 105 g., 65%). Recrystallised several times from water it had m. p. 168·5° (Found: C, 64·3; H, 6·7. $C_{15}H_{18}O_5$ requires C, 64·7; H, 6·5%). The *methyl*, m. p. 37°, b. p. 180—190°/0·05 mm. (Found: C, 66·9; H, 7·1. $C_{17}H_{22}O_5$ requires C,

[6] Prelog, Frenkiel, Kobelt, and Barman, *Helv. Chim. Acta*, 1947, **30**, 1741.

66·7; H, 7·2%), and *ethyl ester*, m. p. 43°, b. p. 190—200°/0·05 mm. (Found: C, 68·7; H, 7·9. $C_{19}H_{28}O_5$ requires C, 68·3; H, 7·8%), were prepared as above.

6-(p-2′-*Carboxyethylphenyl*)*hexanoic Acid*.—The preceding acid (100 g.) was heated in ethylene glycol (350 ml.) with 100% hydrazine hydrate (45 g.) and potassium hydroxide (90 g.) on a water-bath for 4 hr., the temperature raised slowly to the b. p., and refluxing continued for 12 hr. The mixture was cooled, diluted with water (250 ml.), and acidified to Congo-red as usual. The precipitated *acid* was kept at 10° for 1 hr., filtered off, and crystallised from a large volume of water (yield, 71·6 g., 75%). After repeated recrystallisation from water it had m. p. 126·5° (Found: C, 67·9; H, 7·8. $C_{15}H_{20}O_4$ requires C, 68·2; H, 7·5%). The *methyl*, m. p. 27°, b. p. 150—160°/0·06—0·09 mm. (Found: C, 69·5; H, 8·0. $C_{17}H_{24}O_4$ requires C, 69·8; H, 8·3%), and *ethyl ester*, b. p. 165—170°/0·03 mm. (Found: C, 71·4; H, 8·7. $C_{19}H_{28}O_4$ requires C, 71·2; H, 8·7%), were prepared as above. The former with potassium permanganate gave terephthalic acid (dimethyl ester, m. p. 142°).

The author is indebted to Mr. F. Hall for some analyses and to Sir Robert Robinson, O.M., and Dr. G. D. Parkes for their interest and advice.

Dyson Perrins Laboratory, Oxford. [*Received, November 1st*, 1956.]

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423. α-1 : 4-*Glucosans. Part V.* End-group Assay of Glycogens by Periodate Oxidation, and the Oxidation of Maltose by Sodium Metaperiodate.*

By D. J. Manners and (in part) A. R. Archibald.

Fifteen samples of glycogen have been assayed by potassium metaperiodate oxidation, and with only two exceptions, average chain lengths of 10—14 glucose residues were obtained.

Oxidation of glycogen and of maltose, dissolved in sodium chloride, by sodium metaperiodate for 25 hr. at 2° (Potter and Hassid [1]) has been studied. Under these conditions, oxidation is incomplete.

Periodate oxidations have been widely used in structural investigations of polysaccharides, in particular, of starches, glycogens, and dextrans. By estimating the formic acid produced during oxidation, the proportion of triol groups in the polysaccharide can be assessed and, in starches and glycogens, the ratio of non-terminal to non-reducing terminal glucose residues (*i.e.*, average chain length, $\overline{CL}$) determined.[2] Further, examination of an acid hydrolysate of a periodate-oxidised glucosan enables 1 : 2- or 1 : 3-glucosidic linkages to be detected.[3] In the present investigation, the average chain lengths of several samples of glycogen have been determined by (*a*) potassium metaperiodate oxidation at room temperature, and (*b*) sodium metaperiodate oxidation at 2°. A preliminary account of part of this work has been published.[4]

Assay of glycogen by oxidation with potassium periodate was first made by Halsall, Hirst, and Jones,[5] $\overline{CL}$ values being calculated from the production of formic acid after 150 hours' oxidation. Later, Bell and Manners [6] found that samples of mammalian-muscle glycogen ($\overline{CL}$ 12, by methylation) had apparent chain lengths of 15—16 after 150 hours' oxidation. However, when oxidation was continued to maximum production of formic acid (after 300—400 hours' oxidation), $\overline{CL}$ values of 12 ± 1 were obtained. This apparent discrepancy was ascribed to variation in the oxidation rate with room

* Part IV, *J.*, 1956, 2831.

[1] Potter and Hassid, *J. Amer. Chem. Soc.*, 1948, **70**, 3488.
[2] Brown, Dunstan, Halsall, Hirst, and Jones, *Nature*, 1945, **156**, 785.
[3] Hirst, Jones, and Roudier, *J.*, 1948, 1779.
[4] Manners, *Biochem. J.*, 1953, **55**, xx.
[5] Halsall, Hirst, and Jones, *J.*, 1947, 1399.
[6] Bell and Manners, *J.*, 1952, 3641.

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temperature.[7] A similar effect was also noted by Carlquist,[8] who found that in 144 hr. at 15° or 21° a glycogen sample gave 8·4 or 9·5 moles of formic acid per 100 glucose residues. Accordingly, end-group assays have been carried out on 15 different samples of glycogen, and $\overline{CL}$ values, evaluated from the final constant concentrations of formic acid, are recorded in Table 1, together with the specific rotations and methods of preparation of the glycogens.

TABLE 1. *End-group assay of glycogens by oxidation with potassium periodate.*

Source of glycogen [a]	Method of isoln.[b]	Method of purifn.[c]	$[\alpha]_D$ (in H_2O)	$\overline{CL}$	Source of glycogen [a]	Method of isoln.[b]	Method of purifn.[c]	$[\alpha]_D$ (in H_2O)	$\overline{CL}$
Cat liver IV	P	A	—	13	Rabbit liver III...	W	A	+196°	13
Cat liver VI	P	A	—	12	Rabbit liver IV	W	A	—	13
Fœtal pig liver ...	W	A	+191°	11	Rabbit liver V ...	W	A	+196	12
Helix pomatia I ...	P	A	+192	10	Rabbit liver X ...	C	E	+193	12
Helix pomatia II	P	A	+182	7	*Tetrahymena pyriformis* II	P	A	+195	14
Mytilus edulis IV	W	PA	+196	12	*Trichomonas gallinae* II	P	A	+200	13
Mytilus edulis V...	W	A	—	9					
Mytilus edulis VI	C	A	+195	13					
Rabbit liver II ...	P	A	+198	12					

[a] Roman numerals refer to different samples from the same biological source. [b] P = Pflüger method; W = hot-water extraction; C = commercial preparations. [c] A = acetic acid precipitation (Bell and Young, *Biochem. J.*, 1934, **28**, 282); PA = deproteinisation with picric acid; E = electrodialysis.

During isolation of glycogen by the Pflüger method (digestion of the tissues with hot 30% potassium hydroxide), there is no appreciable alkaline-degradation of the polysaccharide.[9] By methylation, the glycogens from rabbit liver III and X and *Helix pomatia* I had chain lengths of 12.[10–12] The latter type of glycogen therefore differs significantly in degree of branching from *Helix pomatia* II glycogen isolated in 1949; the presence of 7-unit chains in this has been confirmed. Fœtal pig liver glycogen, which has not previously been studied, resembles the majority of mammalian glycogens in degree of branching.

An alternative periodate method used by Potter and Hassid [1] involves oxidation at 2° of a solution of the polysaccharide in 1·5% sodium chloride with 1·5 mols. of sodium metaperiodate and determination of the formic acid produced after 25 hr. Chain lengths of 22—27 were reported for various amylopectins, although these results do not appear to have been confirmed by methylation assay of the *same* samples. Other end-group assays of glycogens and amylopectins by this method have been reported;[13–15] the $\overline{CL}$ values were greater than those obtained by other methods of assay of the same samples. In particular, the results differed from enzymic assays (using phosphorylase and amylo-1 : 6-glucosidase), as shown in Table 2.

It appears that with Potter and Hassid's procedure periodate oxidation and, hence, production of formic acid, are incomplete after 25 hr.; it has therefore been applied to glycogens already assayed by potassium periodate. Six samples of glycogen (and one of amylopectin), in sodium chloride solution, were oxidised with sodium metaperiodate at 2°, and the concentration of formic acid was determined after 25 hr. (Table 3). Since the $\overline{CL}$ values from the titres after 25 hr. were greater than those from potassium periodate assay, production of formic acid was incomplete. Six further quantitative experiments

[7] Manners, Ph.D. Thesis, Cambridge, 1952.
[8] Carlquist, *Acta Chem. Scand.*, 1948, **2**, 770.
[9] Greenwood and Manners, *Proc. Chem. Soc.*, 1957, 26.
[10] Bell, *Biochem. J.*, 1935, **29**, 2031.
[11] Haworth and Percival, *J.*, 1932, 2277.
[12] Baldwin and Bell, *Biochem. J.*, 1940, **34**, 139.
[13] Cori and Larner, *J. Biol. Chem.*, 1951, **188**, 17.
[14] Schlamowitz, *ibid.*, p. 145.
[15] Polglase, Smith, and Tyler, *ibid.*, 1952, **199**, 97.
[16] Illingworth, Larner, and Cori, *ibid.*, p. 631; Schlamowitz, personal communication.

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showed that only 80—90% of the theoretical periodate was reduced after 25 hr. Schlamowitz's report [14] that formic acid was completely liberated within 20—25 hr. could not be confirmed (see p. 2209).

The period of 25 hr. for oxidation was chosen by Potter and Hassid [1] on the grounds that their " model " saccharide, maltose, yielded the theoretical 3 mols. of formic acid in this time. Their method is therefore based on the unproved assumption that oxidation of a disaccharide occurs at the same rate as that of a polysaccharide of molecular weight

TABLE 2. *Chain lengths of glycogens and amylopectins determined by periodate oxidation and enzymic methods.*

Sample	Sodium periodate oxidn.*	Enzymic assay	Ref.	Sample	Sodium periodate oxidn.*	Enzymic assay	Ref.
Rabbit liver glycogen	18	14·7	13	Potato amylopectin	27	21·8	13
Rabbit liver glycogen	22	15·9	16	Sago amylopectin ...	22	17	13
Rabbit liver glycogen	23	17·2	16	Wheat amylopectin...	23	18·5	13
Corn amylopectin ...	26	21·2	13				

* Procedure of Potter and Hassid.[1]

TABLE 3. *End-group assays of glycogens by periodate oxidation.*

Sample	Potassium periodate oxidn.*	Sodium periodate oxidn.†		Sample	Potassium periodate oxidn.*	Sodium periodate oxidn.†	
		A	*B*			*A*	*B*
Ascaris lumbricoides	12	15—16	11	*Mytilus edulis* VI...	13	—	14
Cat liver VI	12	—	12	Rabbit liver I	13	—	13
Commercial ‡	—	—	12	Rabbit liver II ...	12	14	—
Helix pomatia II ...	7	9	—	Rabbit liver V ...	12	—	12
Human liver	6	8	—	Rabbit liver X.....	12	—	12
Human muscle ...	12	—	11	*Trichomonas fœtus*	15	18	15
Mytilus edulis V ...	9	13	—				

* See Table 1 and ref. 6. † *A*, Potter and Hassid's procedure; *B*, modified procedure.

‡ Purchased from British Drug Houses Ltd. [waxy maize starch had $\overline{CL}$ values of 18 and 22 by potassium and sodium periodate oxidation (method *A*) respectively].

~10[7]. We have noted, however, that different samples of glycogen are oxidised, under identical conditions, at slightly differing rates. We have re-examined the periodate oxidation of maltose in sodium chloride. In one experiment, after 25 hr. 2·3 mols. of formic acid were produced, and 4·7 mols. of periodate reduced. In additional experiments, maltose, in water or in 3% sodium chloride, was oxidised with varying amounts of sodium metaperiodate. After 25 hr. 1·7—2·6 mols. of formic acid were present, and after *ca.* 120 hr. 2·4—3·1 mols. Although strictly reproducible results could not be obtained in the presence of sodium chloride (see p. 2208), release of formic acid and uptake of periodate were never theoretical after 25 hours' oxidation at 2°.

The formation and subsequent hydrolysis of a formyl ester were incidentally indicated, since production of the third mol. of formic acid continues in the *absence* of periodate. A mixture of maltose in sodium chloride and sodium metaperiodate was divided after 48 hr. at 2° when it contained 2·6 mols. of formic acid. One half was stored at 2° for 24 hr. : the formic acid content increased to 2·9 mols. To the other half ethylene glycol was added, to reduce the remaining periodate, and the formic acid determined immediately and at intervals thereafter. During 24 hr. the formic acid content increased slowly from 2·6 to 2·9 mols. In a similar oxidation by aqueous sodium metaperiodate, we found 2·4 mols. of formic acid released after 48 hours' oxidation, 2·7 mols. after neutralisation of periodate and storage at 2° for 24 hr., and 2·6 mols. after 72 hours' total oxidation. Aliphatic formyl esters are also slowly hydrolysed in presence of sodium metaperiodate at 2° without consumption of periodate. It is apparent that the periodate oxidation of maltose resembles that of lactose [17] and cellobiose,[18] and involves (*a*) an initial oxidation

[17] Meyer and Rathgeb, *Helv. Chim. Acta*, 1948, **31**, 1540.
[18] Head and Hughes, *J.*, 1954, 603.

in which 4 mols. of periodate are reduced and 2 mols. of formic acid produced, and (*b*) a slower stage involving the release of a third mol. of formic acid by hydrolysis of a formyl ester.

The above results on the rate of production of formic acid have been confirmed by others. Morrison and his co-workers [19] found that maltose oxidised by Potter and Hassid's procedure gave 2·5 mols. of formic acid, whilst Potter and his collaborators [20] observed that at 3° the expected 3 mols. of formic acid were not produced after 9 days.

For the end-group assay of glycogens, Potter and Hassid's method has therefore been modified : oxidation in *aqueous* solution is continued for 7—10 days, and the maximum concentration of formic acid determined. With " model " compounds consisting of glycogens already assayed by potassium periodate, the oxidation (determined by periodate-uptake and formic acid production) was normally complete within 7 days. Typical results are reported in Table 3. We noted, however, that with certain mammalian liver glycogens formic acid is produced unexpectedly slowly; [21] the reasons for this are being investigated.

The present study provides further evidence that the *average* length of the chains in glycogens is normally *ca.* 12 glucose residues. We have now assayed some 30 samples of glycogen and, of these, 23 had $\overline{CL}$ values of 10—14. These results agree with those of Abdel-Akher and Smith [22] who for another 37 individual glycogens found average chain lengths of 10—14. This suggests that in most animal tissues the *relative* activity of phosphorylase and branching enzyme during glycogen synthesis is very similar. However, the activity of this enzyme system in different specimens of *Mytilus edulis* appears to vary since glycogens with $\overline{CL}$ values of *ca.* 5, 9, 12, 13, and 17 have been isolated (see Table 1 and ref. 6).

Experimental

Glycogen Samples.—We are indebted to Dr. J. S. D. Bacon for *Mytilus edulis* V glycogen, to Dr. G. D. Greville for the cat liver glycogens, to Dr. E. E. Percival for rabbit liver X glycogen and to Dr. J. F. Ryley for the protozoal glycogens (cf. ref. 23). *Helix pomatia* I glycogen was prepared by deacetylation of the corresponding acetate which was kindly provided by Dr. D. J. Bell. *Mytilus edulis* VI glycogen was purchased from L. Light and Co. Ltd. The remaining samples were isolated and purified as indicated in Table 1. The rotations of 0·2—0·4% glycogen solutions were measured in 2 dm. polarimeter tubes.

Potassium Periodate Oxidation of Glycogens.—The method previously described [6] was used.

Sodium metaperiodate oxidations.

Analytical Methods.—Formic acid was determined, after neutralisation of periodate with ethylene glycol, by titration with 0·01N-sodium hydroxide in a stream of carbon dioxide-free air with (*a*) methyl-red as indicator, when repeating Potter and Hassid's experiments,[1] or (*b*) a glass electrode and pH meter to an end-point at pH 5·8. Periodate uptake was estimated by the methods of Barnebey [24] or Fleury and Lange.[25] Results are expressed as moles per mole of maltose or, for glycogens, moles per mole of anhydroglucose residue.

Oxidations in Presence of Sodium Chloride.—During oxidations of glycogen or maltose in 1·5% sodium chloride solution with sodium metaperiodate, reagent blanks were also analysed. On storage at 2°, these became acid (pH *ca.* 3), and periodate was precipitated. Production of formic acid is therefore calculated from sodium hydroxide titres after correction for the *initial* acidity of the reagent blanks. Further, the results are approximate since the sodium hydroxide titrations include not only release of formic acid by periodate oxidation, but also, and to an unknown extent, acidity due to the interaction of sodium chloride and metaperiodate. The

[19] Morrison, Kuyper, and Orten, *J. Amer. Chem. Soc.*, 1953, **75**, 1502.
[20] Potter, Silveira, McCready, and Owens, *ibid.*, p. 1335; see also Wolff, Hofreiter, Watson, Deatherage, and MacMasters, *ibid.*, 1955, **77**, 1656.
[21] Cf. Perlin, *ibid.*, 1954, **76**, 4101.
[22] Abdel-Akher and Smith, *ibid.*, 1951, **73**, 994.
[23] Manners and Ryley, *Biochem. J.*, 1952, **52**, 480; 1955, **59**, 369.
[24] Barnebey, *J. Amer. Chem. Soc.*, 1916, **38**, 330.
[25] Fleury and Lange, *J. Pharm. Chim.*, 1933, **17**, 107.

precipitation of periodate, which occurred within 24—96 hr., prevented accurate measurement of periodate reduction.

(a) *Glycogens.* Glycogen (30—280 mg.) in 3% sodium chloride (5 ml.) was oxidised with 0·27—0·40M-sodium metaperiodate (5 ml.) at 2° for 25 hr. Ethylene glycol (neutral; 3 ml.) was added, and the mixture kept for 1 hr. at room temperature in the dark, before titration. A control of sodium chloride and metaperiodate was similarly analysed. The results are given in Table 3.

The rate of formic acid production was studied by treating rabbit liver IV glycogen (189·8 mg.) and *Mytilus edulis* I glycogen (110·0 mg.) in 3% sodium chloride (10 ml.) with 0·37M-sodium metaperiodate (10 ml.) at 2° :

Time of oxidn.	Apparent chain length (glucose residues)	
(hr.)	Rabbit liver IV glycogen	*Mytilus edulis* I glycogen
51	16·2	16·2
100	15·0	15·2
166	14·6	14·2
291	12·6	13·2

For measurement of periodate uptake, 50 mg. of glycogen were oxidised for 25 hr. The results were glycogen from *Ascaris lumbricoides*, 0·98 mole per anhydroglucose residue; cat liver IV, 0·89; cat liver VI, 0·94; horse muscle, 0·92; fœtal sheep liver, 0·95, and rabbit liver IV, 0·94. On complete oxidation, these glycogens reduce 1·08—1·09 mols. of periodate.

(b) *Maltose.* Maltose hydrate (223·4 mg.), dissolved in 3% sodium chloride (10 ml.), was oxidised with 0·37M-sodium metaperiodate (10 ml.; 6 mols.) at 2°. The results were :

Time of oxidn. (hr.)	2	4	25	48	72
Formic acid prodn. (mols.)	1·5	1·7	2·3	2·7	3·1

In a second experiment, anhydrous maltose (162·8 mg.) in 3% sodium chloride was treated with 0·27M-sodium metaperiodate (10 ml.; 6 mols.) at 2° :

Time of oxidn. (hr.)	0·5	1	2	22	25	96	145
Periodate uptake (mols.)	3·2	3·9	4·0	4·6	4·7	—	—
Formic acid prodn. (mols.)	1·1	1·2	1·4	2·3	2·3	2·7	3·3

Maltose was also oxidised with varying amounts of sodium metaperiodate (4·4—34·0 mols.); after 25 hr. 1·7—2·5 mols. of formic acid were released, and after 95 hr. 2·5—2·9 mols.

In the above experiments, free iodine was present after *ca.* 90 hr. showing that over-oxidation had occurred.

Oxidations in Absence of Sodium Chloride.—In these oxidations, the reagent control of aqueous sodium metaperiodate was stable on storage at 2°.

(a) *Maltose.* Maltose hydrate (220·4 mg.) in water (10 ml.) was oxidised with 0·37M-sodium metaperiodate (10 ml.; 6 mols.) at 2° with results as follows :

Time of oxidn. (hr.)	2	4	25	48	72
Periodate uptake (mols.)	3·6	—	4·2	4·2	4·4
Formic acid prodn. (mols.)	1·4	1·6	2·2	2·5	2·8

On repetition, 2·1 mols. of formic acid were produced, and 4·2 mols. of periodate consumed after 25 hr. Oxidation of maltose with 4·0 or 11·6 mols. of periodate gave the following results :

Time of oxidn. (hr.)	2	4	25	48	72
Formic acid prodn. (mols.) :					
(*a*) 4·0 mols. of oxidant	1·3	1·4	2·0	2·1	2·3
(*b*) 11·6 mols. of oxidant	1·8	1·9	2·6	2·9	3·0

In the above experiments, the " formic acid " production is slightly lower (*ca.* 0·2 mol. of apparent formic acid) than in those in presence of sodium chloride. The difference is attributed to the acidity developed during the interaction of sodium chloride and metaperiodate.

(b) *Glycogens. Trichomonas fœtus* glycogen [23] (106·4 mg.) in water (25 ml.) was oxidised with 0·37M-sodium metaperiodate (5 ml.) at 2°. Portions (5 ml.) were removed at intervals, ethylene glycol (1 ml.) was added, and the formic acid titrated, with the following results :

Time of oxidn. (days)	2	4	6	10
Formic acid prodn. (mg.)	1·66	1·81	1·93	2·00
Apparent chain length (glucose residues)	18·0	16·4	15·4	15·0

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Under similar conditions, *Ascaris lumbricoides* glycogen (100 mg.) gave 2·26 mg. of formic acid after 3 days, and 2·35 mg. after 5 days; 0·99 and 1·05 mols. of periodate were reduced within 2 and 3 days, respectively.

For end-group assays, glycogen (*ca.* 100 mg.) in water (23 ml.) was oxidised with 0·4M-sodium metaperiodate (2 ml.) at 2°. Portions (5 ml.) were removed at intervals for determination of formic acid. $\overline{CL}$ values, calculated from the final formic acid concentration, are given in Table 3; 1·06—1·09 mols. of periodate were reduced during these oxidations.

Ascaris lumbricoides glycogen (102·5 mg.) and *Mytilus edulis* VI glycogen (95·8 mg.) were also oxidised at room temperature (15—17°). The final production of formic acid (after 8 days) was 2·54 and 2·13 mg. respectively, corresponding to average chain lengths of 11 and 13 glucose residues. During the oxidation of glycogens with a *limited* excess of periodate (*ca.* 30%), appreciable " over-oxidation " does not therefore occur.

Hydrolysis of Formyl Esters.—Mixtures of maltose (*a*) in sodium chloride and (*b*) in water with sodium metaperiodate were divided after 48 hours' oxidation at 2°. One-half of each solution was stored at 2° for a further 24 hr. Ethylene glycol was added to the remaining solutions, which were then titrated with sodium hydroxide (methyl-red). The neutralised solutions were stored at 2° for 24 hr., alkali being added at intervals to maintain the pH. Results were :

Time after redn. of periodate (hr.)	0	2	3	24
Formic acid prodn. (mols.) (*a*)	2·6	2·7	2·8	2·9
(*b*)	2·4	2·5	2·6	2·7

The normal oxidations resulted in the production of (*a*) 2·9 and (*b*) 2·6 mols. of formic acid after 24 hr.

At 2°, and in presence of 3% sodium chloride and 0·37M-sodium metaperiodate, ethyl and *n*-propyl formate were slowly hydrolysed. No periodate was consumed.

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DEPARTMENT OF CHEMISTRY, UNIVERSITY OF EDINBURGH. [*Received, December 19th,* 1956.]

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424. *Formyl Derivatives of Carbazole and* 1 : 2 : 3 : 4-*Tetrahydrocarbazole.*

By P. H. CARTER, (the late) S. G. P. PLANT, and MURIEL TOMLINSON.

The four carbazolealdehydes and the four *Bz*-aldehydes of tetrahydrocarbazole * have been prepared and characterised. Some of their properties are described and their infrared spectra have been measured.

REFERENCES to *Bz*-formylindole derivatives are rare. 4-Formylindole [1] has been described and several 9-alkyl-3-formylcarbazoles have been prepared by Buu-Hoï and Hoán [2] who treated 9-alkylcarbazoles with *N*-methylformanilide and phosphorus oxychloride. We therefore decided to investigate the aldehydes of carbazole and tetrahydrocarbazole.

*cyclo*Hexanone *o*-, *p*-, and *m*-carboxyphenylhydrazones readily afford 5 : 6 : 7 : 8-tetrahydrocarbazole-1-, tetrahydrocarbazole-3-, and a mixture of tetrahydrocarbazole-4- and -2-carboxylic acids, respectively: the mixture can be readily separated by fractional crystallisation.[3,4] These acids formed our obvious starting materials, and we have now shown that their esters can be smoothly dehydrogenated, in quantities up to 5 g., by use

* When not otherwise qualified, tetrahydrocarbazole refers to 1 : 2 : 3 : 4-tetrahydrocarbazole.

[1] Hardegger and Corrodi, *Helv. Chim. Acta*, 1954, **37**, 1826.
[2] Buu-Hoï and Hoán, *J. Amer. Chem. Soc.*, 1951, **73**, 98.
[3] Collar and Plant, *J.*, 1926, 808.
[4] Moggridge and Plant, *J.*, 1937, 1125.

of palladium–charcoal. The substituent is easily lost if the conditions are too vigorous. We found this method preferable to Barclay and Campbell's chloranil method,[5] and thus prepared three of the four methyl carbazolecarboxylates (carbazole-4-carboxylic acid itself does not seem to have been described before).

It has not been possible to prepare the corresponding acid chlorides (compare Murphy and Jenkins [6]) except 1-chloroformylcarbazole which was already known [7] and so we decided to investigate the preparation of the aldehydes by the decomposition of sulphonhydrazides with sodium carbonate in glycol (compare McFadyean and Stevens [8]). It proved possible to make them all by this method. The yields vary considerably and show a correspondence for similar positions of the formyl group in the two series.

1-Formylcarbazole	64%	8-Formyl-1 : 2 : 3 : 4-tetrahydrocarbazole ...	60%
4-Formylcarbazole	67%	5-Formyl-1 : 2 : 3 : 4-tetrahydrocarbazole ...	38·5%
2-Formylcarbazole	34%	7-Formyl-1 : 2 : 3 : 4-tetrahydrocarbazole ...	9·0%
3-Formylcarbazole	7·5%	6-Formyl-1 : 2 : 3 : 4-tetrahydrocarbazole ...	3·2%

Decomposition of 1 : 2 : 3 : 4-tetrahydro-6-, 1 : 2 : 3 : 4-tetrahydro-9-methyl-6-, and 1 : 2 : 3 : 4-tetrahydro-7-(toluene-*p*-sulphonhydrazidocarbonyl)carbazole also affords much of the azine of the expected aldehyde. In addition 3-(toluene-*p*-sulphonhydrazidocarbonyl)carbazole affords some product which seems to be the impure azine. There appears to be no previous reference to the production of azines in this reaction, although Bailey and Staveley [9] isolated an azine as a by-product in a Huang-Minlon decomposition of a semicarbazone, which is a related reaction.

The generalisation, that 2- and 3-substituted carbazoles (and corresponding 7- and 6-substituted tetrahydrocarbazoles) have higher melting-points than the 1- and 4-substituted carbazoles (and 8- and 5-substituted tetrahydrocarbazoles), does not hold with the aldehydes. Infrared absorption shows that there is no hydrogen-bonding in 1-formylcarbazole or 8-formyltetrahydrocarbazole. Small variations in the positions of the CO and NH bands are observed, and the CO band in the spectrum of 2-formylcarbazole shows two maxima.

		Infrared absorption (in Nujol paste).		
Carbazole	M. p.	CO stretching, cm.$^{-1}$	NH stretching, cm.$^{-1}$	Colour
1-Formyl-	143°	1671	3370	Yellow
2- ,, ...	155	1670, 1683	3360	V. pale yellow
3- ,, ...	153—154	1670	3300	Colourless
4- ,, ...	163—164	1679	3200	Yellow
8-Formyltetrahydro-	104	1676	3390	Yellow
7- ,, ...	126—128	1667	3300	Yellow
6- ,, ...	142—144	1670	3230	Colourless
5- ,, ...	144—145	1655	3200	Yellow
6-Formyltetrahydro-9-methyl-	94—95	1671	—	Colourless

These aldehydes are relatively unreactive; they are not readily oxidised by silver nitrate or Fehling's solution, no bisulphite compound has been obtained, and no evidence of a Cannizzaro reaction, "benzoin" condensation, or "mixed benzoin" condensation has been found (although all these reactions have not been attempted with each aldehyde). The common condensation reactions of the formyl group take place normally in most instances. 6-Formyltetrahydrocarbazole is by far the least stable: it is rapidly destroyed in solution. In this it differs from the corresponding 9-methyl compound which suggests that the decomposition is initiated by peroxidation at the 11-position (compare Beer, McGrath, and Robertson [10]). The decomposition product does not liberate iodine from acidified potassium iodide solution so that, if a peroxide is involved, it must disappear rapidly.

[5] Barclay and Campbell, *J.*, 1945, 530.
[6] Murphy and Jenkins, *J. Amer. Pharm. Assoc.*, 1943, **32**, 83.
[7] Manske and Kulka, *Canad. J. Res.*, 1950, **28**, *B*, 443.
[8] McFadyean and Stevens, *J.*, 1936, 584.
[9] Bailey and Staveley, *J. Inst. Petroleum*, 1956, 101.
[10] Beer, McGrath, and Robertson, *J.*, 1950, 2118.

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When 6-formyl-1 : 2 : 3 : 4-tetrahydrocarbazole azine is heated with palladium–charcoal a colourless compound, $C_{26}H_{20}N_2$, which has an ultraviolet absorption spectrum very similar to that of carbazole, is obtained. This may be 1 : 2-dicarbazol-3′-ylethane : it cannot be a dicarbazolylethylene.

Experimental

5 : 6 : 7 : 8-*Tetrahydrocarbazole*-1-*carbohydrazide*.—Ethyl 5 : 6 : 7 : 8-tetrahydrocarbazole-1-carboxylate (11·5 g.) was refluxed with hydrazine (100%; 90 c.c.) for 5 hr. The *hydrazide* (11·9 g.) separated as the solution cooled, and formed prisms (from anisole), m. p. 249—251° (Found: C, 67·8; H, 6·7. $C_{13}H_{15}ON_3$ requires C, 68·1; H, 6·5%). The following were also prepared similarly: 5 : 6 : 7 : 8-*tetrahydrocarbazole*-2-*carbohydrazide*, needles, m. p. 240—241° (from ethanol) (Found: C, 67·9; H, 6·5%); 5 : 6 : 7 : 8-*tetrahydrocarbazole*-3-*carbohydrazide*, prisms, m. p. 200—201° (from aqueous ethanol) (Found: C, 67·9; H, 6·7%); 5 : 6 : 7 : 8-*tetrahydrocarbazole*-4-*carbohydrazide*, needles, m. p. 222—224° (from aqueous ethanol) (Found: C, 68·0; H, 6·6%); 5 : 6 : 7 : 8-*tetrahydro*-9-*methylcarbazole*-3-*carbohydrazide*, needles, m. p. 230—233° (from ethanol) (Found: C, 69·4; H, 6·9. $C_{14}H_{17}ON_3$ requires C, 69·1; H, 7·0%); *carbazole*-1-*carbohydrazide*, plates, m. p. 250—251° (from ethanol) (Found: C, 69·1; H, 5·0. $C_{13}H_{11}ON_3$ requires C, 69·3; H, 4·9%); *carbazole*-2-*carbohydrazide*, prisms, m. p. 276—279° (from acetone) (Found: C, 69·5; H, 5·1%); *carbazole*-3-*carbohydrazide*, prisms, m. p. 261—263° (from ethanol) (Found: C, 69·4; H, 5·2%); and *carbazole*-4-*carbohydrazide*, needles, m. p. 215—217° (from ethanol) (Found: C, 69·2; H, 5·0%).

1 : 2 : 3 : 4-*Tetrahydro*-8-(*toluene*-p-*sulphonhydrazidocarbonyl*)*carbazole*.—The acid hydrazide (11·5 g.) and toluene-*p*-sulphonyl chloride (11 g.) were kept in pyridine for 2 hr. at room temperature. The mixture was then poured into ice and dilute hydrochloric acid and, when it had been dried, the precipitate was recrystallised from ethanol from which 1 : 2 : 3 : 4-*tetrahydro*-8-(*toluene*-p-*sulphonhydrazidocarbonyl*)*carbazole* (10·5 g.) separated as needles, m. p. 210—212° (decomp.) (Found: C, 62·4; H, 5·7. $C_{20}H_{21}O_3N_3S$ requires C, 62·7; H, 5·5%). The following were obtained similarly: 1 : 2 : 3 : 4-*tetrahydro*-7-(*toluene*-p-*sulphonhydrazidocarbonyl*)*carbazole*, prisms, m. p. 242—243° (decomp.) (from ethanol) (Found: C, 62·7; H, 5·7%); 1 : 2 : 3 : 4-*tetrahydro*-6-(*toluene*-p-*sulphonhydrazidocarbonyl*)*carbazole*, prisms, m. p. 240° (decomp.) (from ethanol) (Found: C, 62·9; H, 5·6%); 1 : 2 : 3 : 4-*tetrahydro*-5-(*toluene*-p-*sulphonhydrazidocarbonyl*)*carbazole*, prisms, m. p. 239—241° (decomp.) (from ethanol) (Found: C, 62·7; H, 5·7%); 1 : 2 : 3 : 4-*tetrahydro*-9-*methyl*-6-(*toluene*-p-*sulphonhydrazidocarbonyl*)*carbazole*, plates, m. p. 227—228° (decomp.) (from ethanol) (Found: C, 63·4; H, 5·8. $C_{21}H_{23}O_3N_3S$ requires C, 63·5; H, 5·8%); 1-(*toluene*-p-*sulphonhydrazidocarbonyl*)*carbazole*, prisms, m. p. 236—237° (decomp.) (from acetic acid) (Found: C, 63·2; H, 4·8. $C_{20}H_{17}O_3N_3S$ requires C, 63·3; H, 4·5%); 2-(*toluene*-p-*sulphonhydrazidocarbonyl*)*carbazole*, needles, m. p. 252—255° (decomp.) (from ethanol) (Found: C, 63·4; H, 4·7%); 3-(*toluene*-p-*sulphonhydrazidocarbonyl*)*carbazole*, prisms, m. p. 243—245° (decomp.) (from ethanol) (Found: C, 63·3; H, 4·7%); and 4-(*toluene*-p-*sulphonhydrazidocarbonyl*)*carbazole*, plates, m. p. 265° (decomp.) (from ethanol) (Found: C, 63·4; H, 4·5%). Yields were comparable, except that the 9-methyl compound was obtained in 88% yield.

8-*Formyl*-1 : 2 : 3 : 4-*tetrahydrocarbazole*.—1 : 2 : 3 : 4-Tetrahydro-8-(toluene-*p*-sulphonhydrazidocarbonyl)carbazole (10·2 g.) in ethylene glycol (30 c.c.) was heated in a paraffin-bath to 160° at which temperature anhydrous sodium carbonate (12 g.) was added. Nitrogen was evolved and after 2 min. the mixture was poured into water and extracted with benzene. After it had been dried and concentrated, the benzene layer was passed through activated alumina. The yellow solution from the column afforded 8-*formyl*-1 : 2 : 3 : 4-*tetrahydrocarbazole* (3·2 g.; m. p. 98—102°), yellow needles (from ethanol), m. p. 104° (Found: C, 78·3; H, 6·5; N, 7·4. $C_{13}H_{13}ON$ requires C, 78·4; H, 6·5; N, 7·0%). It failed to give a bisulphite compound, and there was no evidence of any change (Cannizzaro reaction) after treatment with 75% potassium hydroxide solution for 75 hr. The aldehyde was recovered in good yield after it had been boiled with alcoholic potassium cyanide solution for 4 hr. When it was similarly treated with benzoin and potassium cyanide there was no sign of the formation of a mixed benzoin. It did not reduce Fehling's solution, or ammoniacal silver nitrate, or colour Schiff's reagent. It proved impossible to obtain an *N*-acetyl compound. With concentrated sulphuric acid it formed a brick-red solution (other tetrahydrocarbazolealdehydes give brown solutions). 8-Formyltetrahydrocarbazole formed a p-*nitrophenylhydrazone*, orange needles, m. p. 235—237° (from acetic

acid) (Found : C, 68·1; H, 5·6. $C_{19}H_{18}O_2N_4$ requires C, 68·2; H, 5·4%); a 2 : 4-*dinitrophenylhydrazone*, red prisms, m. p. 286° (decomp.) (from anisole) (Found : C, 59·9; H, 4·5. $C_{19}H_{17}O_4N_5$ requires C, 60·1; H, 4·5%); a *semicarbazone*, needles, m. p. 238—239° (from ethanol) (Found : C, 65·9; H, 6·6. $C_{14}H_{16}ON_4$ requires C, 65·6; H, 6·2%); an *azine*, yellow prisms, m. p. 286—288° (from ethanol) (Found : N, 14·2. $C_{26}H_{26}N_4$ requires N, 14·2%); and an *anil*, yellow needles, m. p. 68° (from ethanol), by heating with aniline for 2 hr. (Found : C, 82·9; H, 6·5. $C_{19}H_{18}N_2$ requires C, 83·2; H, 6·6%). Bromination (1 mol.) of 8-formyltetrahydrocarbazole in acetic acid solution, followed by precipitation with water, afforded a *compound*, $C_{13}H_{14}ONBr$, yellow plates (from ethanol), m. p. 134—135° (Found : C, 56·1; H, 5·2; N, 5·0. $C_{13}H_{14}ONBr$ requires C, 55·7; H, 5·0; N, 5·0%).

9-*Acetyl*-8-*cyano*-1 : 2 : 3 : 4-*tetrahydrocarbazole*.—8-Formyltetrahydrocarbazole oxime, prepared in the usual way, failed to crystallise. When it was boiled with acetic anhydride for 1 hr. it afforded 9-*acetyl*-8-*cyano*-1 : 2 : 3 : 4-*tetrahydrocarbazole*, plates, m. p. 169—170° (from benzene) (Found : C, 71·1; H, 5·6. $C_{15}H_{14}O_2N_2$ requires C, 70·8; H, 5·5%).

1 : 2 : 3 : 4-*Tetrahydro*-8-2′-*nitrovinylcarbazole*.—Nitromethane (0·1 g.), 8-formyltetrahydrocarbazole (0·3 g.), and methanol (20 c.c.) were treated at 0° with sodium hydroxide (0·1 g.; in a little water). After ½ hr. the mixture was stirred into ice and hydrochloric acid. 1 : 2 : 3 : 4-*Tetrahydro*-8-2′-*nitrovinylcarbazole* (0·2 g.) separated and was recrystallised from benzene. It separated as red needles, m. p. 230—233° (Found : C, 69·4; H, 5·9. $C_{14}H_{14}O_2N_2$ requires C, 69·4; H, 5·8%).

8-2′-*Acetylvinyl*-1 : 2 : 3 : 4-*tetrahydrocarbazole*.—A mixture of the aldehyde (0·5 g.) and sodium hydroxide (0·06 g., in a little water) in acetone (25 c.c.) gave 8-2′-*acetylvinyl*-1 : 2 : 3 : 4-*tetrahydrocarbazole* (0·3 g.), yellow needles (from ethanol), m. p. 207—208° (Found : C, 80·4; H, 7·3. $C_{16}H_{17}ON$ requires C, 80·3; H, 7·1%).

8-2′-*Carboxyvinyl*-1 : 2 : 3 : 4-*tetrahydrocarbazole*.—The aldehyde (0·5 g.), malonic acid (0·5 g.), piperidine (6 drops), and pyridine (6 c.c.) were heated on a steam-bath until effervescence ceased (3 hr.). The solid obtained by precipitation with dilute hydrochloric acid gave 8-2′-*carboxyvinyl*-1 : 2 : 3 : 4-*tetrahydrocarbazole* (0·3 g.), pale yellow needles (from ethanol), m. p. 223—225° (decomp.) (Found : C, 74·9; H, 6·4. $C_{15}H_{15}O_2N$ requires C, 74·7; H, 6·2%). This acid decolorised alkaline permanganate rapidly and bromine-water slowly. Attempts to esterify it gave a red solid of high m. p.

7-*Formyl*-1 : 2 : 3 : 4-*tetrahydrocarbazole*.—The corresponding toluene-*p*-sulphonhydrazide (15 g.) was decomposed in glycol (50 c.c.) at 160° with anhydrous sodium carbonate (15 g.) as above. The solid formed when the mixture was poured into water was collected and dried. It was only partly soluble in benzene, and the benzene extract, which was chromatographed on alumina, afforded 7-*formyl*-1 : 2 : 3 : 4-*tetrahydrocarbazole* (0·7 g.), yellow needles (from benzene), m. p. 126—128° (Found : C, 78·1; H, 6·5; N, 7·1%; *M*, 194. $C_{13}H_{13}ON$ requires C, 78·4; H, 6·5; N, 7·0%; *M*, 199). The residue, which had not dissolved in benzene, was recrystallised from anisole and gave 7-*formyl*-1 : 2 : 3 : 4-*tetrahydrocarbazole azine* (1 g.), m. p. 315—318°. This was further recrystallised from ethanol and gave yellow prisms, the m. p. of which was not depressed by admixture with a synthetic specimen, m. p. 332°, prepared by refluxing the aldehyde with hydrazine (½ mol.) in alcohol for ½ hr. (Found : C, 79·3; H, 6·6; N, 14·1. $C_{26}H_{26}N_4$ requires C, 79·2; H, 6·6; N, 14·2%). 7-Formyltetrahydrocarbazole gave a 2 : 4-*dinitrophenylhydrazone*, dark red prisms, m. p. 289° (decomp.) (from anisole) (Found : C, 60·0; H, 4·4; N, 18·4. $C_{19}H_{17}O_4N_5$ requires C, 60·1; H, 4·5; N, 18·5%) (this was also obtained from the azine by treatment with 2 : 4-dinitrophenylhydrazine in concentrated sulphuric acid); and an *oxime*, prisms, m. p. 205—207° (from aqueous ethanol) (Found : C, 72·7; H, 6·8; N, 12·7. $C_{13}H_{14}ON_2$ requires C, 72·9; H, 6·5; N, 13·1%). 7-2′-*Acetylvinyl*-1 : 2 : 3 : 4-*tetrahydrocarbazole* was prepared with acetone as above. It formed orange plates, m. p. 175° (from ethanol) (Found : C, 80·4; H, 7·1. $C_{16}H_{17}ON$ requires C, 80·3; H, 7·1%).

6-*Formyl*-1 : 2 : 3 : 4-*tetrahydrocarbazole*.—The corresponding sulphonhydrazide (12 g.) was decomposed as for the preparation of the 7-formyl compound. The benzene extract (which had to be kept from unnecessary contact with air and was used rapidly) yielded 6-*formyl*-1 : 2 : 3 : 4-*tetrahydrocarbazole* (0·2 g.), almost colourless prisms (from benzene), m. p. 142—144° (Found : C, 78·1; H, 6·7; N, 6·8. $C_{13}H_{13}ON$ requires C, 78·4; H, 6·5; N, 7·0%). The solid which did not dissolve in benzene was extracted with alcohol and then recrystallised from anisole giving 6-*formyl*-1 : 2 : 3 : 4-*tetrahydrocarbazole azine*, m. p. 324—327°, identical (mixed m. p.) with a synthetic specimen, plates, m. p. 325—328° (Found : C, 79·2; H, 6·7; N, 13·9. $C_{26}H_{26}N_4$ requires

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C, 79·2; H, 6·6; N, 14·2%). The total yield of azine was about 2 g. Benzene solutions of 6-formyltetrahydrocarbazole rapidly deposit a gum on exposure to air and the aldehyde is destroyed: it was not possible to prepare the aldehyde from the azine, but both the aldehyde and its azine could be converted into a 2 : 4-*dinitrophenylhydrazone*, red prisms, m. p. 286—287° (decomp.) (Found: C, 60·1; H, 4·5; N, 18·4. $C_{19}H_{17}O_4N_5$ requires C, 60·1; H, 4·5; N, 18·5%), and an *oxime*, prisms, m. p. 175—176° (from aqueous ethanol) (Found: C, 72·6; H, 6·5; N, 12·7. $C_{13}H_{14}ON_2$ requires C, 72·9; H, 6·5; N, 13·1%). When this azine was heated with palladised charcoal under carbon dioxide at 330—350°, and the product was sublimed *in vacuo*, a *compound*, $C_{26}H_{20}N_2$ (which may be 1 : 2-dicarbazol-3′-ylethane), was obtained. It crystallised from aqueous ethanol as plates, m. p. 187—188° (Found: C, 86·1; H, 5·7; N, 7·8. $C_{26}H_{20}N_2$ requires C, 86·7; H, 5·5; N, 7·8%).

5-*Formyl*-1 : 2 : 3 : 4-*tetrahydrocarbazole*.—This *compound* was prepared by decomposing the sulphonhydrazide (3·5 g.) as for the 8-formyl compound. It crystallised from benzene as yellow prisms (0·7 g.), m. p. 144—145° (Found: C, 78·2; H, 6·5; N, 7·1. $C_{13}H_{13}ON$ requires C, 78·4; H, 6·5; N, 7·0%). It yielded a 2 : 4-*dinitrophenylhydrazone*, red needles, m. p. 274° (decomp.) (from acetic acid), containing solvent (which could be detected with litmus paper above the melt) (Found: C, 58·9; H, 4·5. $C_{19}H_{17}O_4N_5,\frac{1}{2}C_2H_4O_2$ requires C, 58·7; H, 4·7%). With acetone this aldehyde gave 5-2′-*acetylvinyl*-1 : 2 : 3 : 4-*tetrahydrocarbazole*, yellow prisms, m. p. 241—243° (from ethanol) (Found: C, 80·1; H, 7·2. $C_{16}H_{17}ON$ requires C, 80·3; H, 7·1%).

Methyl 5 : 6 : 7 : 8-*tetrahydro*-9-*methylcarbazole*-3-*carboxylate*.—Methyl 5 : 6 : 7 : 8-tetrahydrocarbazole-3-carboxylate (10 g.) in acetone (200 c.c.) with powdered potassium hydroxide (13·5 g.) was boiled under reflux and treated, during 1 hr., with methyl sulphate (13·6 c.c.) in acetone (13·5 c.c.). After a further hour's boiling the solid was precipitated with water. Recrystallisation from methanol afforded *methyl* 5 : 6 : 7 : 8-*tetrahydro*-9-*methylcarbazole*-3-*carboxylate* (10·2 g.) as prisms, m. p. 157—159° (Found: C, 74·3; H, 7·1. $C_{15}H_{17}O_2N$ requires C, 74·1; H, 7·0%).

6-*Formyl*-1 : 2 : 3 : 4-*tetrahydro*-9-*methylcarbazole*.—Decomposition of the corresponding sulphonhydrazide (12·2 g.) afforded 6-*formyl*-1 : 2 : 3 : 4-*tetrahydro*-9-*methylcarbazole* (0·35 g.; 5·4%), plates [from light petroleum (b. p. 40—60°)], m. p. 94—95° (Found: C, 78·8; H, 7·1; N, 6·8. $C_{14}H_{15}ON$ requires C, 78·8; H, 7·1; N, 6·6%), and the corresponding *azine* (*ca.* 1 g.), m. p. 278—281°. In this instance the azine dissolved in benzene and was eluted from the alumina after the aldehyde. It was identical with the azine (yellow prisms; m. p. 278—281°) prepared from the aldehyde and recrystallised from anisole (Found: N, 13·4. $C_{28}H_{30}N_4$ requires N, 13·3%). 6-*Formyltetrahydro*-9-*methylcarbazole* 2 : 4-*dinitrophenylhydrazone* crystallised from anisole as red prisms, m. p. 288° (decomp.) (Found: C, 60·7; H, 4·7. $C_{20}H_{19}O_4N_5$ requires C, 61·1; H, 4·9%).

Methyl Carbazole-2-*carboxylate*.—Methyl 5 : 6 : 7 : 8-tetrahydrocarbazole-2-carboxylate (5 g.) and palladium–charcoal (1·3 g., containing 5% of Pd) were heated at 280° under carbon dioxide until effervescence was no longer vigorous (about 10 min.). The residue was extracted with acetone, and water precipitated *methyl carbazole*-2-*carboxylate* (4 g.), plates (from methanol), m. p. 175—177° (Found: C, 74·7; H, 5·0. $C_{14}H_{11}O_2N$ requires C, 74·7; H, 4·9%). *Methyl carbazole*-3-*carboxylate* (4·0 g.) was obtained in the same way from the corresponding tetrahydro-compound (5·0 g.), and was obtained as prisms, m. p. 169—171° (from methanol) (Found: C, 74·3; H, 4·9%), as was *methyl carbazole*-4-*carboxylate*, needles, m. p. 96—97° [from light petroleum (b. p. 60—80°)] (Found: C, 74·2; H, 4·9%). Hydrolysis of the latter with aqueous methanolic sodium hydroxide (30 min.) gave *carbazole*-4-*carboxylic acid*, prisms, m. p. 244—245° (from benzene) (Found: C, 74·2; H, 4·4. $C_{13}H_9O_2N$ requires C, 73·9; H, 4·3%).

1-*Formylcarbazole*.—Decomposition of the corresponding sulphonhydrazide (5·5 g.) afforded 1-*formylcarbazole* (1·8 g.), yellow prisms, m. p. 143° (from ethanol) (Found: C, 80·1; H, 4·7; N, 7·4. $C_{13}H_9ON$ requires C, 80·0; H, 4·6; N, 7·2%). It gave a 2 : 4-*dinitrophenylhydrazone*, red prisms, m. p. 301—303° (decomp.) (from anisole) (Found: C, 61·0; H, 3·7. $C_{19}H_{13}O_4N_5$ requires C, 60·8; H, 3·5%); a *semicarbazone*, plates, m. p. 315—318° (from anisole) (Found: C, 66·8; H, 5·0. $C_{14}H_{12}ON_4$ requires C, 66·7; H, 4·8%); and an *azine*, yellow plates, m. p. 325—326° (from anisole) (Found: N, 14·6. $C_{26}H_{18}N_4$ requires N, 14·5%). From it also were prepared 1-2′-*acetylvinylcarbazole*, yellow prisms, m. p. 188—190° (from ethanol) (Found: N, 5·6. $C_{16}H_{13}ON$ requires N, 6·0%); and 1-2′-*carboxyvinylcarbazole*, yellow needles, m. p. 249° (decomp.) (from acetic acid) (Found: C, 75·7; H, 4·7. $C_{15}H_{11}O_2N$ requires C, 75·9; H, 4·6%). Its solution in concentrated sulphuric acid was a characteristic cherry-red.

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2-*Formylcarbazole*.—This *compound* (0·4 g.) was obtained from the sulphonhydrazide (2 g.). It formed pale yellow needles, m. p. 155° (from benzene) (Found: C, 79·7; H, 4·6; N, 7·5. $C_{13}H_9ON$ requires C, 80·0; H, 4·6; N, 7·2%). It gave a 2 : 4-*dinitrophenylhydrazone*, red prisms, m. p. 328° (decomp.) (Found: C, 60·5; H, 3·5. $C_{19}H_{13}O_4N_5$ requires C, 60·8; H, 3·5%), but an attempt to make the azine gave only the *hydrazone*, prisms, m. p. above 340° (Found: C, 74·5; H, 5·3. $C_{13}H_{11}N_3$ requires C, 74·6; H, 5·3%). Both these derivatives are extremely sparingly soluble and separated pure from the reaction mixture. 2-Formylcarbazole gives a brown solution in sulphuric acid.

3-*Formylcarbazole*.—Decomposition of the sulphonhydrazide (5·2 g.) gave 3-*formylcarbazole* (0·2 g.), prisms, m. p. 153—154° (from aqueous ethanol) (Found: C, 79·7; H, 4·8; N, 7·2. $C_{13}H_9ON$ requires C, 80·0; H, 4·6; N, 7·2%), together with a solid (about 1·5 g.), which it was impossible to recrystallise and which is almost certainly the impure azine. The *azine*, prisms, m. p. 356° (Found: N, 14·0. $C_{26}H_{18}N_4$ requires N, 14·5%), and the red 2 : 4-*dinitrophenylhydrazone*, prisms, m. p. 326—328° (decomp.) (Found: C, 60·8; H, 3·8. $C_{19}H_{13}O_4N_5$ requires C, 60·8; H, 3·5%), were prepared: both were too insoluble to be recrystallised. With acetone this aldehyde gave 3-2′-*acetylvinylcarbazole*, yellow needles, m. p. 160—162° (Found: N, 5·9. $C_{16}H_{13}ON$ requires N, 6·0%). 3-Formylcarbazole gives a brownish-red solution in sulphuric acid.

4-*Formylcarbazole*.—The sulphonhydrazide (3·2 g.) gave 4-*formylcarbazole* (1·1 g.), yellow prisms, m. p. 163—164° (from benzene) (Found: C, 80·0; H, 4·8; N, 7·2. $C_{13}H_9ON$ requires C, 80·0; H, 4·6; N, 7·2%). It gave an *anil*, pale yellow needles, m. p. 151° (from ethanol) (Found: C, 84·4; H, 5·4; N, 9·9. $C_{19}H_{14}N_2$ requires C, 84·4; H, 5·2; N, 10·4%): the 2 : 4-*dinitrophenylhydrazone*, red prisms, m. p. 300° (decomp.) (Found: C, 60·7; H, 3·4. $C_{19}H_{13}O_4N_5$ requires C, 60·8; H, 3·5%), and the *azine*, yellow prisms, m. p. 305—307° (Found: N, 14·3. $C_{26}H_{18}N_4$ requires N, 14·5%), crystallised as they were prepared, and were not sufficiently soluble to be recrystallised. A solution of 4-formylcarbazole in sulphuric acid is brick-red.

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425. *Studies in Relation to Biosynthesis. Part XI.* The Structure of Nalgiovensin.*

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Examination of the infrared and ultraviolet spectra of nalgiovensin, triacetylnalgiovensin, and the products of oxidation of these substances with chromic acid leads to the formula (I; R = CH_2·CHMe·OH) for nalgiovensin, in accord with prediction on the basis of its probable biosynthesis from acetic acid.

IN Part V [1] was discussed the possible origin from acetic acid of many anthraquinones derived from fungi and some from higher plants. Successful use of this hypothesis in structural determinations of anthraquinones related to emodin, the triphenol corresponding to (I; R = Me), would support its validity in the anthraquinone field.

Nalgiovensin was shown by Raistrick and Ziffer [2] to be (I; R = CHEt·OH, CH_2·CHMe·OH, or CHMe·CH_2·OH). The positions of the oxygen atoms attached to the nucleus strongly suggest an acetic acid origin (II) and if the side-chain is similarly derived the most probable formula will be (I; R = CH_2·CHMe·OH).

Oxidation of the optically active nalgiovensin, $C_{18}H_{16}O_6$, by chromic acid gives an inactive substance, dehydronalgiovensin, $C_{18}H_{14}O_6$, presumably the ketone produced by

* Part X, Birch and Moye, *J.*, 1957, 412.

[1] Birch and Donovan, *Austral. J. Chem.*, 1955, **8**, 529.

[2] Raistrick and Ziffer, *Biochem. J.*, 1951, **49**, 563.

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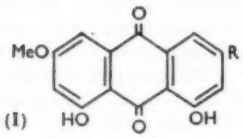
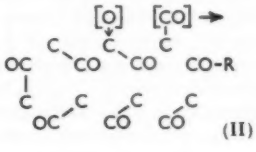
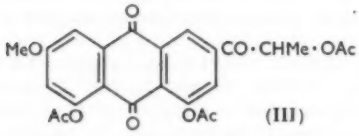
oxidation of the alcohol group. This structure is confirmed by (i) appearance of a new infrared carbonyl band at 1722 cm.$^{-1}$ (in $CHCl_3$), which can only be due to a carbonyl group in an unconjugated position, β or γ in the side-chain, and (ii) the very similar ultraviolet spectra (in EtOH) of nalgiovensin and the ketone in the region 200—400 mμ, indicating that the new carbonyl group is not adjacent to the ring. Similar oxidation of triacetylnalgiovensin, $C_{24}H_{22}O_9$, gives an optically inactive compound, $C_{24}H_{22}O_{11}$ or, more probably, $C_{24}H_{20}O_{10}$ (III) resulting from oxidation to a carbonyl group of a methylene group adjacent



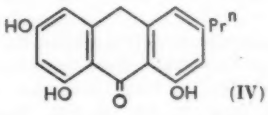
(I)



(II)



(III)



(IV)

to the aromatic ring (the racemisation is due to the position of the asymmetric centre adjacent to the new carbonyl group). The latter structure is supported by the markedly different ultraviolet spectra of triacetylnalgiovensin and its oxidation product, and a new infrared carbonyl band at 1705 cm.$^{-1}$ (in $CHCl_3$), some 17 cm.$^{-1}$ lower than that of the saturated carbonyl group in dehydronalgiovensin—the carbonyl group is therefore conjugated with the ring system. The vinyl acetate bands are at 1772 cm.$^{-1}$ in both triacetylnalgiovensin and triacetyloxonalgiovensin, but the alcoholic acetate band in the latter has shifted from 1731 to 1740 cm.$^{-1}$ by introduction of the new carbonyl group.

Nalgiovensin is reduced by hydriodic acid [2] to an anthrone which must be (IV) (or the corresponding anthranol) since, after oxidation with chromic acid and steam-distillation, paper chromatography of the volatile acids [3] showed the presence of acetic, propionic, and *n*-butyric acid.

The combined evidence proves that nalgiovensin is (I; R = CH_2·CHMe·OH) as expected, and strengthens the view that it and related substances are derived biochemically from acetic acid.

Experimental

The mould used was *Penicillium nalgiovensis* Lax., obtained from Kew and grown according to the literature.[2] The dried mycelium (60 g.) was continuously extracted with chloroform for 24 hr., the extract was evaporated to dryness, and the fats were removed by refluxing four times with light petroleum (b. p. 40—60°). The residue was dissolved in chloroform, and most of the nalgiolaxin removed by four extractions with N-sodium carbonate. The chloroform solution was evaporated to a small volume and chromatographed on magnesium silicate (Magnesol)–Celite (1 : 1) in ethyl acetate. Fairly pure nalgiovensin was obtained directly from the yellow eluate, the remaining nalgiolaxin staying on the column. Recrystallisation [2] gave nalgiovensin (400 mg.), m. p. 199·5—200·5°. The derivatives were prepared by the published routes.[2]

Infrared spectra in the region 5·5—6·5 μ (0·25% solutions in $CHCl_3$) were :

Nalgiovensin : 1615s, 1630s, 1680m, 1725w.

Dehydronalgiovensin : 1615s, 1630s, 1680m, 1722s.

Triacetylnalgiovensin : 1606s, 1675s, 1731s, 1772s.

Triacetyloxonalgiovensin : 1605s, 1675s, 1705s, 1740s, 1772s.

[3] Garbers, Schmid, and Karrer, *Helv. Chim. Acta*, 1954, **37**, 1336.

Ultraviolet spectra in EtOH were:

Nalgiovensin: max. at 225, 266, 287, 437 mμ (ε 33,800, 18,500, 16,700, 12,200); min. at 237, 276, 331 mμ (10,000, 15,700, 1290).

Dehydronalgiovensin: max. at 225, 266, 287, 437 mμ (ε 34,400, 17,900, 17,000 12,700); min. at 238, 277, 332 mμ (ε 11,500, 16,100, 2500).

Triacetylnalgiovensin: max. at 271, 346 mμ (ε 35,000, 4780); min. at 232, 311 mμ (ε 11,500, 2940).

Triacetyloxonalgiovensin: max. at 225, 243, 275, 350 mμ (ε 24,700, 25,100, 29,500, 5800); min. at 232, 258, 316 mμ (ε 23,700, 20,200, 3400).

Oxidation of Anthrone (IV).—The anthrone (IV) (25·4 mg.) was oxidised according to the method of Garbers, Schmid, and Karrer.[3] The volatile acids obtained as the mixed ethylamine salts were chromatographed on paper in butanol–water.[4] Spots were obtained corresponding to acetic (R_F 0·20), propionic (R_F 0·31), and *n*-butyric (R_F 0·49) acid; authentic acids run for comparison gave spots of identical R_F values.

We are indebted to the University of Manchester for a Science Research Scholarship (to R. A. M.-W.) and to Dr. G. D. Meakins for advice on infrared spectra.

CHEMISTRY DEPARTMENT, MANCHESTER, 13. [*Received, January 19th*, 1957.]

[4] Lindquist and Storgards, *Acta Chem. Scand.*, 1953, **7**, 87.

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426. *Alkylperoxy-radicals. Part III.* Kinetics of Autoxidations Retarded by Aromatic Amines.*

By A. F. BICKEL and E. C. KOOYMAN.

The relative reactivities at 60° of various aromatic amines were determined by measuring initial rates of oxidation in a system involving reactions of alkylperoxy-radicals with an amine (AH) or with a standard hydrocarbon (RH = 9 : 10-dihydroanthracene). The initiating radicals were produced by thermal dissociation of 2 : 2 : 3 : 3-tetraphenylbutane and reaction of the resulting radicals with oxygen.

Several types of kinetics were found to occur, depending on the amine investigated and were interpreted on the assumption that amines react in the same way as alkylphenols. Attempts to isolate definite compounds were unsuccessful.

Secondary aromatic amines can be characterized in the same manner as alkylphenols, (1) by the efficiency, *i.e.*, the ratio of the rates of hydrogen abstraction by alkylperoxy-radicals from the amine and from the hydrocarbon respectively, and (2) by the rate of the chain-transfer reaction $A\cdot + RH \longrightarrow AH + R\cdot$. The antioxidant efficiencies of these two classes of compound appeared to be of the same order of magnitude. The presence of large *N*-naphthyl groups completely prevented the occurrence of chain transfer.

Tertiary amines showed no retarding properties but *increased* the rate of oxygen-absorption, indicating the formation from the amine of active radicals capable of adding oxygen.

AN insight into the mode of action of alkylphenols as antioxidants was obtained earlier by kinetic investigations of autoxidations retarded by these compounds, as described in Part II.* This work was based on the isolation of the products formed by reaction of the phenols with alkylperoxy-radicals.[1] We have now investigated similarly the mechanism of oxidations retarded by aromatic amines.

The competitive system described in Part II was again employed for the quantitative comparison of the reactivities of the amines. The isolation of products formed by interaction of amines and independently generated alkylperoxy-radicals, however, proved to

* Part II, *J.*, 1956, 2215.

[1] Part I, *J.*, 1953, 3211.

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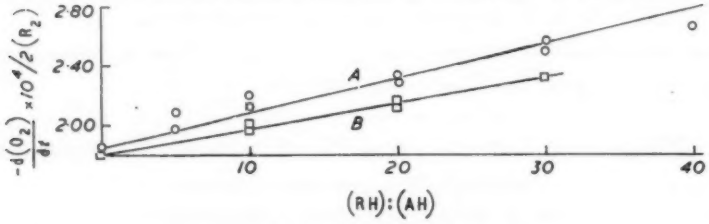
be extremely difficult. As a result, the interpretation of the kinetic measurements is not as well founded as in the case of the phenolic antioxidants. In many instances, however, the kinetics were comparable to those found for phenols, which makes it possible to draw plausible conclusions about mechanism.

The isolation of products was attempted : (1) by dissociation of 2 : 2 : 3 : 3-tetraphenylbutane in a solution of the amine in the presence of oxygen, and (2) by decomposition of *tert.*-butyl hydroperoxide by cobalt naphthenate in a solution of the amine. Both methods, when applied to *N*-phenyl-β-naphthylamine, yielded a small amount of an oxygen-containing compound that may be a hydroxy-derivative of the amine. In other cases only tars were produced. These negative results stand in contrast to the high yields of products obtained from phenols (Part I) ; the difference may be due to a greater reactivity towards RO·O· of the primary reaction products of RO·O· and amine.

FIG. 1. *A*, N-*Phenyl-β-naphthylamine*. *B*, N-*Phenyl-α-naphthylamine*.



Kinetics.—The kinetics were studied by measuring initial rates of oxygen consumption as a function of intakes of 9 : 10-dihydroanthracene (RH) as standard hydrocarbon, aromatic amine (AH) as retarder, 2 : 2 : 3 : 3-tetraphenylbutane (R_2) as initiator and bromobenzene as inert solvent. The merits of this system as well as the assumptions involved were discussed in Part II. Moreover, the measurement of *initial rates* minimizes the kinetic importance of secondary processes which may play a dominant role in the isolation experiments.

From the results it appeared that the amines can be arranged in several groups showing different kinetic behaviours : (*a*) for *N*-phenyl-α- and -β-naphthylamine the initial rate of oxidation is a roughly linear function of the (RH) : (AH) ratio * (Fig. 1). (*b*) The initial rates of oxidation retarded by *N*-methylaniline and aniline are linear functions of 1/(AH) (Fig. 2) as well as of (RH) (Fig. 3) ; they may be represented as a linear function of (RH)/(AH) + *c*(RH), where *c* is a constant. (*c*) Oxidations inhibited by *NN'*-di-*sec.*-butyl-*p*-phenylenediamine show a true induction period, the length of which depends on (AH) (Table 2). (*d*) *NN*-Dimethylaniline and triethylamine accelerate oxidation of the standard hydrocarbon. If a system of initiator, *tert.*-amine, and 2 : 6-di-*tert.*-butyl-4-methylphenol as retarder is employed the amine behaves as a chain-carrying hydrocarbon.

The main reactions in the competitive system will be the following : †

$$R_2 \xrightarrow{k_D} 2R\cdot \qquad R\cdot + O_2 \longrightarrow RO\cdot O\cdot$$

$$RO\cdot O\cdot + RH \xrightarrow{k_r} RO\cdot OH + R\cdot$$

$$RO\cdot O\cdot + AH \xrightarrow{k_h} RO\cdot OH + A$$

* Parentheses in such expressions and in the mathematical expressions denote concentrations in moles per 300 ml. (446 g.) of bromobenzene, this being the volume used in all experiments (cf. *J.*, 1956, 2216, footnote) ; $d(O_2)/dt$ is in moles/sec.

† In these formulations R· produced in dissociation is $Ph_2MeC\cdot$, but in general the free radical R· is 10-hydro-9-anthryl. This difference does not affect radical-propagation but would be material if products were under consideration.

antioxidant and hydrocarbon competing for the alkylperoxy-radicals. Termination may be effected by interaction of A· radicals, *e.g.*, dimerization,

$$2A\cdot \xrightarrow{k_d} A_2$$

The rate of oxidation is then given by eqn. (1) of Part II :

$$-d(O_2)/dt = 2k_D(R_2)\{1 + k_r(RH)/k_b(AH)\} \quad . \quad . \quad . \quad . \quad . \quad (1)$$

With regard to (*a*) above, the retarding action of the *N*-phenylnaphthylamines can therefore be interpreted in terms of this simple mechanism. The type of products formed being unknown, other terminations such as $RO\cdot O\cdot + A\cdot \longrightarrow RO\cdot OA$ may also be involved; they result in a similar linear dependency of rate on (RH) : (AH) ratio. The antioxidant

FIG. 2. *Aniline*: *A*, (RH) = 5·0 × 10⁻³; *B*, (RH) = 2·0 × 10⁻³. *N-Methylaniline*: *C*, (RH) = 5·0 × 10⁻³; *D*, (RH) = 2·0 × 10⁻³.

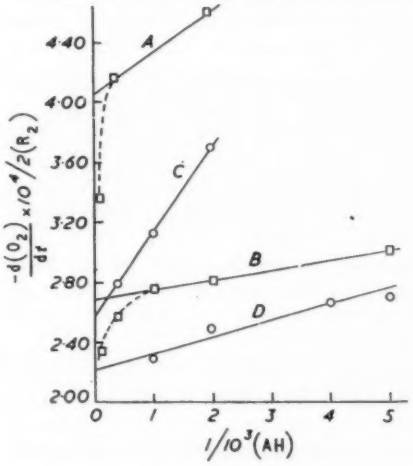
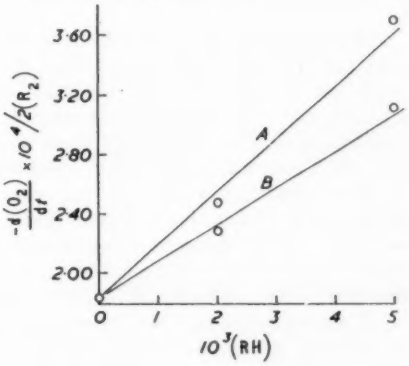


FIG. 3. *N-Methylaniline*: *A*, (AH) = 0·5 × 10⁻³; *B*, (AH) = 1 × 10⁻³.



efficiencies, k_b/k_r, can be evaluated from the slope of the lines in Fig. 1 and are presented in Table 1, where, for comparison, the values of two phenols have been included.

With regard to (*b*) above, *N*-methylaniline probably acts in accordance with the above kinetics including a chain-transfer reaction :

$$A\cdot + RH \xrightarrow{k_c} AH + R\cdot$$

The rate of oxidation is represented by :

$$-d(O_2)/dt = 2k_D(R_2)\{1 + k_r(RH)/k_b(AH)\} + k_c\{2k_D(R_2)/k_dV\}^{\frac{1}{2}}(RH) \quad . \quad (2)\ *$$

For (RH) = constant, eqn. (2) becomes :

$$-d(O_2)dt = c_1 + c_2(AH)^{-1} \quad . \quad . \quad . \quad . \quad . \quad . \quad (3)$$

The antioxidant efficiency k_b/k_r can be determined from the slopes of plots of eqn. (3)

* This is the correct form of eqn. (7) of Part II.

(Fig. 2). The values of c_1 can be used to calculate $k_c/k_d^{\frac{1}{2}}$, a measure of the chain transfer. For (AH) = constant, eqn. (2) becomes :

$$-d(O_2)/dt = c_3 + c_4(RH) \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (4)$$

In a plot of $-d(O_2)/dt$ against (RH), the intercept is the same for all values of (AH) (Fig. 3).

The results for aniline (Fig. 2) point to the same mechanism, an exception being the behaviour at high concentrations of aniline, the initial rates of oxidation then being lower than correspond to the equation. This suggests the formation by dimerization from aniline of a more efficient antioxidant, for instance an aminodiphenylamine.

TABLE 1.

	Antioxidant efficiency	Chain transfer		Antioxidant efficiency	Chain transfer
α-$C_{10}H_7$·NHPh	104 *	0	NHPhMe	15 *	0·03 †
β-$C_{10}H_7$·NHPh	80 *	0	NH_2Ph	~40 *	~0·07 †
4 : 2 : 1-$C_6H_3MeBu^t$-OH	118	0	*p*-$C_6H_4Bu^t$-OH	80—100	0·0085 †
			p-$C_6H_4(NHBu^s)_2$	>10,000	—

* k_b/k_r. † $k_c/k_d^{\frac{1}{2}}$.

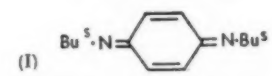
With respect to (*c*) above, *NN'*-di-*sec.*-butyl-*p*-phenylenediamine shows behaviour that has not yet been encountered among alkylphenols. Its action can probably be explained by assuming the operation of the simple mechanism for the phenylnaphthylamines, with the additional condition $k_b \gg k_r$; the oxidation chain involving the hydrocarbon will only be established when nearly all the amine has been consumed. This true inhibition makes it impossible to calculate the antioxidant efficiency in the usual fashion. A lower limiting value can be estimated in the following manner. At a ratio (RH) : (AH) = 400 : 1 the initial rate is less than 4% higher than that for the single initiator. A 4% increase in initial rate would imply an efficiency of 10,000; the actual value may be even higher. The practical value of this extremely efficient antioxidant, however, is limited by its instability towards oxygen.

It appears that the amount of inhibitor present is approximately equal to the amount of initiator decomposed in the induction period (Table 2). Hence it follows that *two*

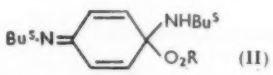
TABLE 2. 2 : 2 : 3 : 3-*Tetraphenylbutane* : 1 *mmole*; 9 : 10-*dihydroanthracene* : 20 *mmoles*.

Induction period (min.)	Initiator decomposed (mmole)	Amine (mmole)	Induction period (min.)	Initiator decomposed (mmole)	Amine (mmole)
3·9	0·047	0·050	10·4	0·121	0·150
7·8	0·093	0·100	>20	—	0·250

alkylperoxy-radicals are inactivated per inhibitor molecule, a fact which points either to dehydrogenation to a quinone imide (I) or to the formation of a peroxide (II) :



(I)



(II)

With regard to (*d*) above, tertiary amines are attacked by alkylperoxy-radicals with the production of chain-propagating radicals. This follows from experiments carried out in the absence of 9 : 10-dihydroanthracene, the rate of oxidation being increased by an increase of the amine concentration. We have tried to gain some insight into the oxidation of tertiary amines by employing them as oxidizable substrate and retarding their oxidation by different amounts of a hindered phenol, such as 2 : 6-di-*tert.*-butyl-4-methylphenol. It appeared that the initial rate of oxidation can be represented as a

nearly linear function of $(RH)^{\frac{1}{2}}/(AH)^{\frac{1}{2}}$ for triethylamine and of $(RH)^{\frac{1}{2}}/(AH)$ for dimethylaniline. These results cannot be interpreted in terms of a simple mechanism. The oxidation of *NN*-dimethylaniline may follow a pattern similar to that described by Horner *et al.*[2] for its reaction with benzoyl peroxide. Kinetic schemes based on the formation of $PhMeN{\cdot}CH_2{\cdot}$ and $PhMeN{\cdot}CH_2{\cdot}O{\cdot}O{\cdot}$ as chain-carrying radicals lead, however, to relations between the rate of oxidation and (RH) and (AH) that differ essentially from that found experimentally. A complete analysis of the products formed in the oxidation appears to be an essential condition for a better knowledge of the mechanism.

Relations between Structure and Reactivity of Aromatic Amines.—Antioxidant efficiencies of alkylphenols and secondary aromatic amines have the same order of magnitude. It is assumed that their respective reactions with alkylperoxy-radicals follow a similar pattern, the first step probably being the removal of hydrogen from the amino-group. This hydrogen abstraction will be interfered with by the shielding effect of bulky groups bound to the nitrogen. On the other hand, conjugating groups such as β-naphthyl in *N*-phenyl-β-naphthylamine will contribute more to the resonance stabilization of the radical than to that of the amine itself, thus causing a lowering of the N–H bond strength compared with that of amines not having this extra conjugation, for instance, *N*-methylaniline. Attack of alkylperoxy-radicals on the naphthylamine is considerably faster than on *N*-methylaniline. Apparently the conjugative effect of β-naphthyl predominates over its classical steric hindrance.

Both the shielding effect and the lower strength of the N–H bond to be formed will be responsible for the absence of a chain-transfer reaction $A{\cdot} + RH \longrightarrow AH + R{\cdot}$ with the phenylnaphthylamines.

The extremely large antioxidant efficiency of *NN'*-di-*sec.*-butyl-*p*-phenylenediamine can, at least in part, be explained by a weakened N–H bond combined with the large polar effect of the *p*-$NHBu^s$ group.[3,4]

Experimental (with W. Roest)

Starting Materials.—*N*-Phenyl-α- and β-naphthylamine, recrystallized from ethanol, had m. p. 61·5—62·0° and 107·5—108·5° respectively.

Triethylamine, aniline, *N*-methylaniline, *NN*-dimethylaniline, and *NN'*-di-*sec.*-butyl-*p*-phenylenediamine were fractionated and had b. p. 88·5—89·0°, 181·5—182·5°, 77·7—78·7°/13 mm., 80·8—81·5°/17 mm., and 173·5—174·5°/17 mm., respectively.

Other starting materials were prepared as described in Parts I and II.

Reactions of N-*Phenyl*-β-*naphthylamine with* tert.-*Butyl Hydroperoxide and Cobalt Naphthenate or with* 2 : 2 : 3 : 3-*Tetraphenylbutane and Oxygen.*—These reactions were performed by procedures similar to those described in Part I. A very small amount of a colourless *substance*, m. p. 167—167·5°, was isolated by percolation of the evaporated reaction mixture over aluminium oxide and recrystallization from toluene–ethanol (Found: C, 82·1; H, 6·1; N, 5·6. $C_{16}H_{13}ON$ requires C, 81·7; H, 5·6; N, 5·9%).

Initial rates of oxidation were determined in the manner given in Part II.

Koninklijke/Shell-Laboratorium, Amsterdam. [*Received, September 19th,* 1956.]

[2] Horner *et al.*, *Annalen*, 1950, **566**, 69; 1953, **579**, 175, 193.
[3] Russell, *J. Amer. Chem. Soc.*, 1956, **78**, 1047.
[4] Kooyman, van Helden, and Bickel, *Proc. Ned. Akad. Wet.*, 1953, *B*, **56**, 75.

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427. *The Chemistry of Bacteria. Part IV.* A C_{20}-Acid from Violacein.*

By J. A. Ballantine, C. B. Barrett, R. J. S. Beer, B. G. Boggiano, K. Clarke, Stephen Eardley, B. E. Jennings, and Alexander Robertson.

Reductive hydrolytic fission of violacein gives, in high yield, a colourless acid, $C_{20}H_{16}O_5N_2$, which on the basis of chemical and spectroscopic evidence is formulated as a γ-(5-hydroxy-3-indolyl)-α-oxindolyl-γ-oxobutyric acid (VII).

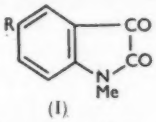
In earlier papers of this series it has been argued that violacein, the pigment of *Chromobacterium violaceum*, contains a 5-hydroxyindole nucleus, an oxindole nucleus, and probably a hydroxypyrrole residue. The present communication is concerned with the structure of a colourless acidic degradation product, $C_{20}H_{16}O_5N_2$, obtained from violacein by the action of alkali in the presence of zinc. If, as now seems likely, the molecular formula of violacein proves to be of the type C_{21}–N_3 (see Part III *), then only one carbon atom and one nitrogen atom are lost in the formation of this C_{20}-acid, a conclusion which is consistent with the high yield of the acid and with the simultaneous production of ammonia, identified as toluene-*p*-sulphonamide, during the degradation.

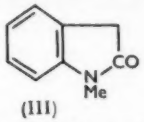
The behaviour of the C_{20}-acid with methylating agents showed that it is a phenolic acid containing two other weakly acidic replaceable hydrogen atoms. Thus with diazomethane the acid gave a phenolic methyl ester (a monomethyl derivative) which, rather surprisingly, was also formed by the action of methyl iodide and potassium carbonate in boiling acetone. With methyl sulphate and an excess of alkali the C_{20}-acid gave an acidic trimethyl derivative containing one methoxyl group, whilst the use of an excess of methyl sulphate, so that the reaction mixture finally became acidic, yielded a neutral tetramethyl derivative with two methoxyl groups. The latter compound is clearly the methyl ester of the trimethyl derivative, from which it was prepared by methyl iodide–potassium carbonate. The position of the methyl groups in the trimethyl derivative is established by the oxidation with potassium permanganate to 1-methylisatin (I; R = H) and 5-methoxy-1-methylisatin (I; R = OMe). The C_{20}-acid therefore contains the 5-hydroxyindole and oxindole residues believed to be present in violacein. Of the four carbon atoms unaccounted for, one is present as a carboxyl, and a second must occur as a carbonyl group since the tetramethyl derivative of the C_{20}-acid forms a 2 : 4-dinitrophenylhydrazone; the parent acid does not give satisfactory carbonyl derivatives. Further evidence that the C_{20}-acid contains a keto-acid system is provided by condensation of the trimethyl derivative and hydrazine with the loss of two molecules of water to give a non-acidic product which must be either a pyrazolone or a pyridazinone. The same compound is also obtained from the tetramethyl derivative with, in this case, the elimination of a molecule of water and of methanol. The properties of the C_{20}-acid are not those of a β-keto-acid. Thus, it is stable to hot alkali in the absence of oxygen and is not readily decarboxylated. Under vigorous conditions for decarboxylation, extensive decomposition occurs and the main product is 5-hydroxyindole. We consider that the C_{20}-acid is a γ-keto-acid and must contain system (II) with linked oxindole and 5-hydroxyindole nuclei, an arrangement which is in agreement with the absence of a *C*-methyl group (Kuhn–Roth determination).

The stability of the C_{20}-acid to alkaline hydrolysis indicates that the carbonyl group in expression (II) is not attached to the oxindole nucleus, since 3-acyloxindoles are alkali-sensitive. The carbonyl group must therefore be linked to the indole nucleus, in either the α- or the β-position. That it is attached to the β-position is indicated partly by the oxidation experiments described later and partly by spectroscopic studies. Thus, the 2 : 4-dinitrophenylhydrazone of the tetramethyl derivative is a deep red compound ($\lambda_{max.}$

* Part III, *J.*, 1954, 2679.

431 mμ in $CHCl_3$) very similar in colour to the dinitrophenylhydrazone of 1 : 2 : 3 : 4-tetrahydro-9-methyl-4-oxocarbazole [1] ($\lambda_{max.}$ 436 mμ in $CHCl_3$). Moreover the ultraviolet absorption of the C_{20}-acid and its derivatives can be very satisfactorily interpreted as


(I)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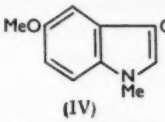
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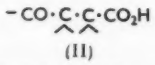

(II)

simple summations of absorptions due to oxindole and β-acylindole residues. As illustrated in the Table the absorption characteristics of an equimolar mixture of 1-methyloxindole (III) and γ-(5-methoxy-1-methyl-3-indolyl)-γ-oxobutyric acid [1] (IV) are almost identical with those of the tetramethyl derivative and, similarly, a mixture of 1-methyloxindole and the pyridazinone [1] derived from the acid (IV) shows virtually the same ultraviolet absorption as does the pyridazinone obtained from the trimethyl derivative of the C_{20}-acid. The differences between the ultraviolet absorption characteristics of α- and β-acylindoles are marked [1] and it is therefore possible to eliminate an α-acylindole structure for the C_{20}-acid.

	$\lambda_{max.}$ (mμ) (log ε)	$\lambda_{min.}$ (mμ) (log ε)
Equimolar mixture of (III) and (IV)	253 (4·36), 306 (3·95)	233 (3·93), 285 (3·85)
Tetramethyl deriv. of C_{20}-acid	255 (4·39), 308 (4·05)	287 (3·92)
Equimolar mixture of (III) and the pyridazinone from (IV)	265 (4·28), 278 (4·27), 327 (4·30)	244 (4·17), 272 (4·24), 290 (4·00)
Pyridazinone obtained from trimethyl-deriv. of C_{20}-acid	266 (4·28), 280 (4·26), 328 (4·30)	245 (4·18), 275 (4·23), 292 (4·01)

The infrared absorption spectra of the C_{20}-acid and its derivatives are consistent with formulation of the acid as a β-acylindole having attached carboxyl and oxindolyl groups. The tetramethyl derivative, for example, has four well-defined peaks in the carbonyl region at 1736, 1695, 1631, and 1610 cm.$^{-1}$, of which those at 1695 and 1610 cm.$^{-1}$ may be attributed to the oxindole system (oxindole, 1695, 1610 cm.$^{-1}$; 1-methyloxindole, 1695, 1605 cm.$^{-1}$); the peak at 1736 cm.$^{-1}$ is assigned to the carbonyl of the methoxycarbonyl group, and that at 1631 cm.$^{-1}$ to the carbonyl of a 1-methyl-3-acylindole (characteristic value,[1] 1620—1640 cm.$^{-1}$). The C_{20}-acid and its methyl ester have ill-defined peaks at *ca.* 3200 cm.$^{-1}$ but these cannot be assigned to NH groups in β-acylindole systems [1] since oxindole absorbs in the same region (3165 cm.$^{-1}$).

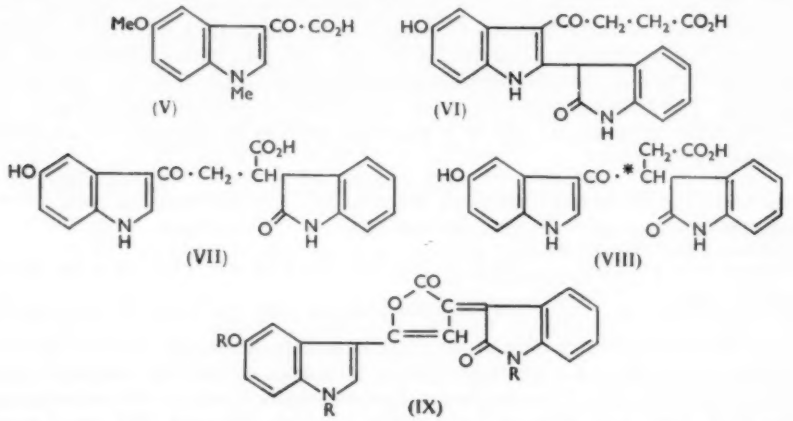
Early in these investigations it was observed that the C_{20}-acid was converted by hot acetic anhydride and sodium acetate into a non-acidic red product, the " red lactone," analyses of which indicated that three acetyl groups had been introduced and that a molecule of water and, probably, two atoms of hydrogen had been lost. Under similar conditions the trimethyl derivative of the C_{20}-acid also gave a red product (the " magenta lactone "), again with the loss of a molecule of water, the disappearance of acidic properties, and the probable loss of two hydrogen atoms. The tetramethyl derivative, with no free carboxyl group, was unattacked by the acetylating mixture, and the monomethyl ester gave a *colourless* product which could not be satisfactorily purified. Thus the formation of a neutral red product in these reactions requires the presence of a carboxyl group which is presumably involved in a cyclisation eliminating water.

Oxidation of the " red lactone " gave *N*-acetylanthranilic acid and isatin as the only identified products, but a similar oxidation of the " magenta lactone " afforded not only 1-methylisatin and 5-methoxy-1-methylisatin, but also 5-methoxy-1-methyl-3-indolylglyoxylic acid (V) which was isolated as its methyl ester. In view of this result it must be regarded as unlikely that in the C_{20}-acid the oxindole nucleus is directly attached to the α-position of the 5-hydroxyindole system as in (VI).

Of the two remaining possible structures (VII) and (VIII), to be considered for the

[1] Ballantine, Barrett, Beer, Boggiano, Eardley, Jennings, and Robertson, following paper.

C_{20}-acid, (VII) is preferable for two reasons. If violacein contains a hydroxyindolylpyrrylmethene structure,[2] the the γ-keto-acid system (II) is formed from the pyrrole ring and the methene carbon atom (with loss of one carbon atom and ammonia). The reconstruction of a normal pyrrylmethene from the keto-acid system of (VIII) is impossible; the carbon atom marked * would have to be quaternary in violacein and would effectively block the extensive conjugation necessary to produce the colour of the pigment. This objection does not apply to structure (VII). A second reason for rejecting structure (VIII) arises from a consideration of the nature of the red cyclisation products (lactones) obtained from the C_{20}-acid and its trimethyl derivative. On the basis of structure (VII) for the C_{20}-acid, these products can be satisfactorily formulated as (IX; R = Ac or Me), which



accounts for the loss of acidic properties and for the observed dehydration; it is assumed that the oxidation permitted by the analyses brings about the conversion of an oxindolyl into an oxindolidene group, a change which should give rise to colour, especially in the environment represented by (IX). A study [3] of various model compounds, for example an analogue of (VII) in which the 5-hydroxyindole nucleus is replaced by a phenyl group, strongly supports these views.

We are unable to devise an equally satisfactory formulation for these products on the basis of structure (VIII).

Methyl 5-methoxy-1-methyl-3-indolylglyoxylate, required for comparison with the oxidation product described above, was synthesised by two independent methods. 5-Methoxyindole was readily converted into the glyoxylic acid by reaction with oxalyl chloride and hydrolysis of the intermediate acid chloride. With methyl sulphate and alkali the acid gave both 5-methoxy-1-methyl-3-indolylglyoxylic acid (V) and its methyl ester, which was also obtained from the glyoxylic acid by conventional esterification methods. The interaction of 5-methoxy-3-indolylglyoxylyl chloride and methanol furnished methyl 5-methoxy-3-indolylglyoxylate and with methyl sulphate this ester also yielded methyl 5-methoxy-1-methyl-3-indolylglyoxylate. The same product was prepared from 5-methoxy-1-methylindole by a Hoesch reaction with methyl cyanoformate.

Experimental

Unless otherwise stated the light petroleum employed had b. p. 60—80°.

Ultraviolet absorption spectra refer to EtOH solutions (Unicam spectrophotometer), and infrared data were obtained with a Grubb-Parsons double-beam spectrometer and a paste of the compound in "Nujol."

[2] Beer, Jennings, and Robertson, *J.*, 1954, 2679.
[3] Unpublished results from this laboratory.

Degradation of Violacein with Zinc and Alkali.—A mixture of violacein (1·0 g.), zinc dust (2·0 g.), and 2N-aqueous sodium hydroxide (100 ml.) was heated under reflux in nitrogen for 45 min., then decanted from undissolved zinc, which was washed with a little water. The combined liquors were neutralised (pH 6·5—7) with concentrated hydrochloric acid and, after removal of the precipitated zinc salts, acidified, giving a pale yellow solid (*ca.* 700 mg.). Recrystallised from acetone–light petroleum (b. p. 40—60°), this gave the C_{20}-*acid* in small colourless needles (500—650 mg.), m. p. 252—254° (decomp.) (Found: C, 65·7; H, 4·7; N, 8·0%; equiv., 371, 368. $C_{20}H_{16}O_5N_2$ requires C, 65·9; H, 4·4; N, 7·7%; *M*, 364). In one experiment, the evolved basic gas was collected in 2N-hydrochloric acid and converted into its toluene-*p*-sulphonyl derivative which crystallised from ethyl acetate–light petroleum in colourless plates, m. p. and mixed m. p. with toluene-*p*-sulphonamide, 136°.

Alkyl Derivatives of the C_{20}-*Acid.*—A slight excess of ethereal diazomethane was added to a solution of the C_{20}-acid (200 mg.) in methanol (50 ml.), and 15 min. later the solvents were evaporated *in vacuo*. Trituration of the residue with aqueous sodium hydrogen carbonate left the *methyl ester* which on repeated recrystallisation from ethyl acetate–light petroleum formed colourless needles (170 mg.), m. p. 247—249° (Found: C, 66·1; H, 5·3; N, 7·5; OMe, 8·1, 8·4. $C_{19}H_{15}O_3N_2{\cdot}CO_2Me$ requires C, 66·7; H, 4·8; N, 7·4; OMe, 8·2%). The same ester (90 mg.) was obtained by heating the acid (200 mg.) with methyl iodide and potassium carbonate in boiling acetone.

Addition of methyl sulphate (2·5 ml.) portion-wise (0·5 ml.) to a warm agitated solution of the C_{20}-acid (250 mg.) in 2N-aqueous sodium hydroxide (17 ml.) (nitrogen atmosphere) during 45 min. gave, after acidification of the cooled mixture, the *trimethyl derivative* (250 mg.) which was washed with cold acetone and then crystallised from acetone, forming colourless plates (200 mg.), m. p. 266—267° (decomp.) [Found: C, 67·5, 67·7; H, 5·8, 5·5; N, 6·8; OMe, 7·6%; equiv., 404, 410. $C_{21}H_{18}O_2N_2(OMe){\cdot}CO_2H$ requires C, 68·0; H, 5·4; N, 6·9; OMe, 7·6%; *M*, 406].

Methylation of the C_{20}-acid (1·0 g.), in the presence of 2N-aqueous sodium hydroxide (30 ml.), with an excess of methyl sulphate (7·5 ml.) so that the mixture eventually became acidic, gave the neutral *tetramethyl derivative* (900 mg.) which separated from alcohol in colourless needles, m. p. 181° [Found: C, 68·5, 68·7; H, 6·0, 6·0; N, 6·45; OMe, 15·5. $C_{21}H_{18}O_2N_2(OMe){\cdot}CO_2Me$ requires C, 68·6; H, 5·7; N, 6·7; OMe, 14·8%]. The same product, m. p. and mixed m. p. 180—181°, was obtained by the action of methyl iodide and potassium carbonate on the trimethyl derivative in boiling acetone. The 2:4-*dinitrophenylhydrazone* crystallised from benzene–light petroleum in red prisms, m. p. 228—230° (decomp.) (Found: C, 59·6; H, 4·7; N, 13·7. $C_{30}H_{22}O_8N_6$ requires C, 60·0; H, 4·7; N, 14·0%).

Acetylation of the C_{20}-*Acid.*—The acid (100 mg.), acetic anhydride (4 ml.), and sodium acetate (100 mg.) were heated under reflux for 15 min., and 12 hr. later the "*red lactone*" [4-(5-*acetoxy*-1-*acetyl*-3-*indolyl*)-2-(1-*acetyl*-3-*oxindolidene*)-4-*hydroxybut*-3-*enoic lactone*] was collected, washed with water, and crystallised from benzene, forming deep red needles (30 mg.), m. p. *ca.* 286° (decomp.) [Found: C, 66·7; H, 4·0; N, 5·8; Ac, 26·8. $C_{20}H_9O_4N_2(CO{\cdot}CH_3)_3$ requires C, 66·4; H, 3·8; N, 6·0; Ac, 27·4%]. Acetylation by the acetic anhydride–pyridine method (5 days at 0°) gave an inseparable mixture of red and colourless products.

The deep magenta solution obtained by heating a mixture of the trimethyl derivative (100 mg.) of the C_{20}-acid, anhydrous sodium acetate (100 mg.) and acetic anhydride (3 ml.) under reflux for 10 min. slowly deposited a neutral product (*ca.* 30 mg.), the "*magenta lactone*" [4-*hydroxy*-4-(5-*methoxy*-1-*methyl*-3-*indolyl*)-2-(1-*methyl*-3-*oxindolene*)*but*-3-*enoic lactone*], which crystallised from benzene in deep magenta plates with a green reflex, m. p. 268—270° (decomp.), and does not contain an acetyl residue (Found: C, 71·9; H, 7·2; N, 6·8. $C_{23}H_{18}O_4N_2$ requires C, 71·5; H, 4·7; N, 7·3%). Under the same conditions, the tetramethyl derivative of the C_{20}-acid was recovered unchanged.

Oxidation of the "Magenta Lactone" from the Trimethyl Derivative of the C_{20}-*Acid.*—A stirred solution of the lactone (880 mg.) in boiling acetone (1 l.) was cooled rapidly and, before crystallisation began, powdered potassium permanganate (1·3 g.) was added in portions. The precipitated manganese dioxide was removed and the dark red solid left after evaporation of the liquor was extracted with boiling water, giving a mixture of pale orange needles and clusters of red needles, which was separated in the first instance by chromatography from benzene on talc, but more successfully by careful fractional sublimation in a high vacuum. Thus were obtained (*a*) 1-methylisatin (bath-temp. 80—90°/0·005 mm.), m. p. 130°, which crystallised

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from benzene–light petroleum in pale orange prisms, m. p. and mixed m. p. 134° (Found: C, 67·3; H, 4·6. Calc. for $C_9H_7O_2N$: C, 67·1; H, 4·4%) and (*b*) 5-methoxy-1-methylisatin (bath-temp. 100—110°/0·005 mm.), m. p. *ca.* 170°, which formed dark red needles, m. p. and mixed m. p. 175—176°, from benzene–light petroleum (Found: C, 62·7; H, 4·8. Calc. for $C_{10}H_9O_3N$: C, 62·9; H, 4·7%). The manganese dioxide precipitate was extracted with hot water (3 × 20 ml.) and, on acidification, the extracts afforded a pale brown acidic solid (100 mg.). More acidic material was obtained by continuous ether-extraction of the acidified aqueous extracts. The combined acidic fractions were esterified with ethereal diazomethane and on distillation the product gave two fractions: (*a*) a trace of colourless oil (bath-temp. 120—140°/0·01 mm.) and (*b*) a pale yellow oil (bath-temp. 140—180°/0·01 mm.) which became partly crystalline. Fraction (*b*) was redistilled (bath-temp. 130—140°/0·001 mm.) and, on crystallisation from acetone–light petroleum, then gave methyl 5-methoxy-1-methyl-3-indolylglyoxylate in pale yellow prisms, m. p. and mixed m. p. 133° (Found: C, 62·4; H, 5·3; N, 5·7; OMe, 25·7. Calc. for $C_{13}H_{13}O_4N$: C, 63·1; H, 5·3; N, 5·7; OMe, 25·1%).

Oxidation of the "Red Lactone" from the C_{20}-Acid.—Slow addition of potassium permanganate (235 mg.) in acetone (30 ml.) to a stirred cold solution of the lactone (210 mg.) in the same solvent (200 ml.) gave isatin, m. p. and mixed m. p. 198—200°, isolated from the acetone solution, and *N*-acetylanthranilic acid, isolated by water-extraction of the manganese dioxide formed in the oxidation and identified by conversion into the methyl ester, m. p. and mixed m. p. 97—98°.

Oxidation of the Trimethyl Derivative of the C_{20}-Acid.—Potassium permanganate (1·0 g.), in acetone (200 ml.), was added slowly to a stirred solution of the trimethyl derivative of the C_{20}-acid (1·0 g.) in the same solvent (1200 ml.) at 40°. The precipitated manganese dioxide was collected and washed with acetone, and the filtrate and washings were combined, decolorised with sulphur dioxide, and evaporated. A solution of the residue in benzene was washed with aqueous sodium hydrogen carbonate, dried, and evaporated, leaving bright crystals which by careful distillation in a pistol were resolved into 1-methylisatin (82 mg.) and 5-methoxy-1-methylisatin (71 mg.).

Attempted Decarboxylation of the C_{20}-Acid.—The mixture obtained by heating the C_{20}-acid (500 mg.) and copper bronze in glycerol (10 ml.) to 260—270° for 10 min. was diluted with water (40 ml.), filtered, and extracted with ether. The brown gum left on evaporation of the ether was boiled with hot light petroleum and, on cooling, the extract deposited 5-hydroxyindole (60 mg.) in colourless needles, m. p. and mixed m. p. 106—107°. On sublimation (bath-temp. 180°/0·001 mm.) the residue, insoluble in light petroleum, afforded a crystalline product, which separated from acetone–light petroleum in colourless cubes (15 mg.), m. p. 265° (Found: C, 69·2; H, 5·5; N, 7·9%). The latter product, which formed a deep red 2 : 4-dinitrophenylhydrazone and a crystalline acetyl derivative, m. p. *ca.* 190°, was also obtained in small yield in other attempted decarboxylations.

Interaction of the Trimethyl Derivative of the C_{20}-Acid and Hydrazine.—The colourless *pyridazinone* (200 mg.), obtained by heating a solution of the trimethyl derivative (200 mg.) in alcohol (15 ml.) with 90% hydrazine hydrate (1 ml.) for 8 hr., separated from 95% alcohol in long colourless needles, m. p. 242° (Found: C, 68·5; H, 5·6; N, 13·8. $C_{23}H_{22}O_3N_4$ requires C, 68·6; H, 5·5; N, 13·9%). The same product was formed in a similar reaction with the tetramethyl derivative of the C_{20}-acid.

5-Methoxy-3-indolylglyoxylic Acid.—Prepared from ethyl 5-methoxyindole-2-carboxylate,[4] 5-methoxyindole-2-carboxylic acid [5] was decarboxylated to 5-methoxyindole. Addition of oxalyl chloride (0·75 ml.) to a solution of 5-methoxyindole (0·70 g.) in ether (15 ml.) gave 5-methoxy-3-indolylglyoxylyl chloride [6] (1·0 g.) as an orange-red solid, m. p. 130°. A solution of this compound (0·50 g.) in warm 2N-aqueous potassium hydroxide (100 ml.) was cooled and acidified with dilute hydrochloric acid; crystallised from ethyl acetate, the resulting *5-methoxy-3-indolylglyoxylic acid* formed yellow prisms (300 mg.), m. p. 248° (Found: C, 60·2; H, 4·3; N, 6·1. $C_{11}H_9O_4N$ requires C, 60·3; H, 4·1; N, 6·4%).

Methyl 5-Methoxy-1-methyl-3-indolylglyoxylate.—(*A*) A solution of potassium hydroxide (1·5 g.) in water (4·5 ml.) was added to 5-methoxy-3-indolylglyoxylic acid (0·30 g.) in acetone (30 ml.), followed by methyl sulphate (2·5 ml.) added in 20 min. with constant shaking.

[4] Hughes and Lions, *J. Proc. Roy. Soc., N.S.W.*, 1937, **71**, 475.
[5] Blaikie and Perkin, *J.*, 1924, **125**, 296.
[6] Speeter and Antony, *J. Amer. Chem. Soc.*, 1954, **76**, 6209.

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20 Min. later the colourless solid which had separated at the interface of the two layers was collected and dissolved in water. On acidification the solution gave *5-methoxy-1-methyl-3-indolylglyoxylic acid* which crystallised from ethyl acetate in bright yellow needles (0·20 g.), m. p. 194° (Found: C, 61·5; H, 4·8; N, 6·1. $C_{12}H_{11}O_4N$ requires C, 61·8; H, 4·7; N, 6·0%). On evaporation the acetone-rich layer from the methylation mixture left an oil which slowly solidified in contact with cold water. Recrystallised from ethyl acetate–light petroleum this afforded *methyl 5-methoxy-1-methyl-3-indolylglyoxylate* in yellow prisms (0·075 g.), m. p. 133—134° (Found: C, 63·1; H, 5·3; N, 5·9; OMe, 24·7. $C_{13}H_{13}O_4N$ requires C, 63·2; H, 5·3; N, 5·7; OMe, 25·1%). The same ester was obtained by the action of diazomethane on the glyoxylic acid or by evaporation of a solution of the acid in methanol containing a trace of concentrated hydrochloric acid.

(*B*) By the action of methanol (4 ml.) in ether (35 ml.) 5-methoxy-3-indolylglyoxylyl chloride (0·50 g.) was converted into *methyl 5-methoxy-3-indolylglyoxylate* which formed yellow plates (0·45 g.), m. p. 255°, from acetone (Found: C, 61·7; H, 4·9; N, 6·0. $C_{13}H_{11}O_4N$ requires C, 61·8; N, 4·7; N, 6·0%). With methyl sulphate in an aqueous acetone solution of potassium hydroxide this ester (0·3 g.) gave methyl 5-methoxy-1-methyl-3-indolylglyoxylate (0·23 g.), m. p. and mixed m. p. 134°.

(*C*) A solution of 5-methoxy-1-methylindole [7] (1·0 g.) and methyl cyanoformate (1·5 ml.) in ether (10 ml.) at 0° was saturated with hydrogen chloride and kept for 12 hr. at 0—5°. The crystalline ketimine hydrochloride was collected, and decomposed with warm very dilute aqueous sodium carbonate; the resulting methyl 5-methoxy-1-methyl-3-indolylglyoxylate, crystallised from acetone–light petroleum, had m. p. and mixed m. p. 134°.

5-Methoxy-1-methylisatin.—*5-Methoxy-1-methylisatin* was prepared by methylation of 5-methoxyisatin,[8] in 50% aqueous methanol (40 ml.), with methyl sulphate (2·5 ml.) and sufficient 2N-aqueous sodium hydroxide to maintain neutrality, and was isolated with benzene. It separated from water and then from benzene–light petroleum in dark red needles (0·07 g.), m. p. 175—176° (Found: C, 62·5; H, 4·8. $C_{10}H_9O_3N$ requires C, 62·8; H, 4·7%).

UNIVERSITY OF LIVERPOOL. [*Received, November 26th*, 1956.]

[7] Julian, *J. Amer. Chem. Soc.*, 1949, **71**, 3206; 1951, **73**, 970.
[8] Bachman and Picha, *ibid.*, 1946, **68**, 1601.

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428. *The Chemistry of Bacteria. Part V.*[1] *Some Acylindoles.*

By J. A. BALLANTINE, C. B. BARRETT, R. J. S. BEER, B. G. BOGGIANO, STEPHEN EARDLEY, B. E. JENNINGS, and ALEXANDER ROBERTSON.

In connection with an investigation on the constitution of a C_{20}-acid (I) derived from violacein the ultraviolet and infrared absorption spectra of a number of acylindoles of types (II), (III), and (IV) have been examined.

THE assignment of structure (I) to the C_{20}-acid [1] derived from violacein depends partly on a spectroscopic comparison of the compound with various acylindoles which have been prepared as models. The present paper collects the available data on these compounds which include (*a*) simple 3-acylindoles, 3-acyl-5-methoxyindoles, and 1 : 2 : 3 : 4-tetrahydro-4-oxocarbazole, all represented by the generalised expression (II), (*b*) 2-acetyl-3-methylindole and some 1 : 2 : 3 : 4-tetrahydro-1-oxocarbazoles (III), and (*c*) a group of compounds represented by (IV). Since they contain the γ-keto-acid system the compounds in the latter group are close models of the C_{20}-acid.

Ultraviolet absorption data for the acylindoles are given in Table 1. Compounds of type (II) each have three absorption maxima of roughly equal intensity. When the 5-position is unsubstituted (II; R = H) the maxima appear at *ca.* 240, 265, and 300 mμ, whilst the 5-methoxyindoles (II; R = OMe) have maxima at *ca.* 255, 280, and 300 mμ. The indolyl-oxobutyric acid group (type IV) shows essentially the same characteristics,

[1] Part IV, Ballantine, Barrett, Beer, Boggiano, Clarke, Eardley, Jennings, and Robertson, preceding paper.

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although in one example the central maximum is missing and in two other cases it appears as a shoulder. The 2-acylindoles (type III), on the other hand, have quite different absorption curves, with two high-intensity maxima at *ca.* 235 and 310 mμ and a pronounced minimum at *ca.* 265 mμ.

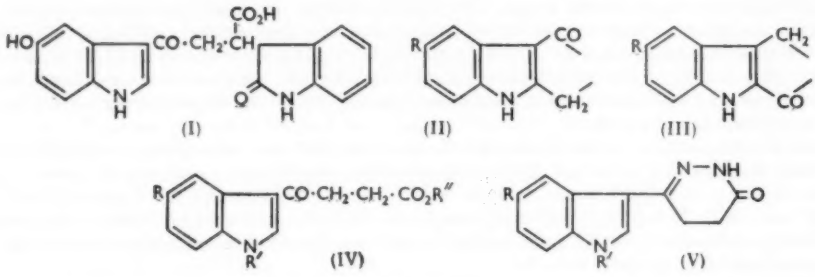

Table 2 lists the important peaks in the infrared absorption spectra of some of the acylindoles. It will be observed that the absorption maxima due to the ketone groups in the 3-acylindoles which have a free NH group fall within the range 1590—1620 cm.$^{-1}$, whilst the 3-acyl-1-methylindoles have peaks between 1620 and 1640 cm.$^{-1}$. The two α-acylindoles for which data are available have a carbonyl gand at 1630 cm.$^{-1}$. The NH (stretching) peaks in 3-acylindoles appear between 3130 and 3220 cm.$^{-1}$, at rather lower frequencies than the characteristic range for simple indoles [2] (3330—3500 cm.$^{-1}$). The two 2-acylindoles have peaks at 3247 and 3311 cm.$^{-1}$ respectively.

The acylindoles required for this study were prepared either by methods already described or by suitable modifications of conventional procedures. It has become clear

TABLE 1. *Ultraviolet absorption spectra of acylindoles.*

Type	Compound	$\lambda_{max.}$ (mμ) (log ε)	$\lambda_{min.}$ (mμ) (log ε)
3-Acyl	3-Acetyl-2-methylindole	240 (4·02), 266 (3·92), 300 (3·98)	225 (3·77), 254 (3·79), 279 (3·83)
	2-Methyl-3-phenylacetylindole	244 (4·17), 268 (4·07), 303 (4·13)	229 (3·95), 255 (3·95), 281 (3·96)
	1 : 2 : 3 : 4-Tetrahydro-4-oxocarbazole	242 (4·26), 265 (4·16), 295 (4·10)	224 (3·85), 251 (3·98), 279 (3·97)
	3-Acetyl-5-methoxy-2-methylindole	254 (4·07), 278 (4·00), 301 (4·00)	234 (3·88), 263 (3·94), 292 (3·96)
	5-Methoxy-2-methyl-3-phenylacetylindole	255 (4·23), 278 (4·14), 303 (4·12)	234 (3·77), 265 (4·03), 289 (4·06)
	γ-(3-Indolyl)-γ-oxobutyric acid	242 (4·01), 298 (4·10), shoulder, 259 (3·95)	271 (3·78)
	γ-(1-Methyl-3-indolyl)-γ-oxobutyric acid	245 (4·15), 304 (4·14)	272 (3·65)
	γ-(5-Methoxy-3-indolyl)-γ-oxobutyric acid	252 (4·20), 268 (4·03), 303 (4·02)	263 (4·02), 283 (3·89)
	γ-(5-Methoxy-1-methyl-3-indolyl)-γ-oxobutyric acid	255 (4·25), 307 (4·04), shoulder, 273 (3·99)	235 (3·69), 284 (3·82)
2-Acyl	2-Acetyl-3-methylindole	238 (4·17), 312 (4·33)	265 (2·98)
	1 : 2 : 3 : 4-Tetrahydro-1-oxocarbazole	236 (4·31), 307 (4·46)	263 (3·03)
	1 : 2 : 3 : 4-Tetrahydro-6-methoxy-1-oxocarbazole	232 (4·22), 314 (4·44)	265 (3·13)
	1 : 2 : 3 : 4-Tetrahydro-6 : 7-dimethoxy-1-oxocarbazole	231 (4·21), 334 (4·43)	267 (3·04)

that 3-acylindoles are readily methylated at the NH group with methyl sulphate and alkali and this method has normally been used for the preparation of 3-acyl-1-methylindoles. The methyl esters of the γ-indolyl-γ-oxobutyric acids (type IV) were condensed with hydrazine, yielding indolylpyridazinones (V) which served as models for a product [1]

[2] Bellamy, "The Infra-red Spectra of Complex Molecules," Methuen, London, 1954, p. 215.

of similar structure prepared from the trimethyl and tetramethyl derivatives of the C_{20}-acid. Details of the ultraviolet absorption spectra of these pyridazinones are collected in Table 3.

TABLE 2. *Infrared absorption spectra.*

Type	Compound	NH region ($cm.^{-1}$)	Carbonyl region ($cm.^{-1}$)
3-Acyl	3-Acetyl-2-methylindole	3135	1597
	3-Acetyl-5-methoxy-2-methylindole	3134	1601, 1618
	1 : 2 : 3 : 4-Tetrahydro-4-oxocarbazole	3165	1592
	1 : 2 : 3 : 4-Tetrahydro-9-methyl-4-oxocarbazole	—	1626
	γ-(3-Indolyl)-γ-oxobutyric acid	3220	1684 (CO_2H), 1621
	Methyl γ-(3-indolyl)-γ-oxobutyrate	3155	1742 (CO_2Me), 1618
	γ-(1-Methyl-3-indolyl)-γ-oxobutyric acid	—	1690 (CO_2H), 1621
	Methyl γ-(1-methyl-3-indolyl)-γ-oxobutyrate	—	1710 (CO_2Me), 1627
	γ-(5-Methoxy-3-indolyl)-γ-oxobutyric acid	3155	1733 (CO_2H), 1613
	γ-(5-Methoxy-1-methyl-3-indolyl)-γ-oxobutyric acid	—	1712 (CO_2H), 1639
2-Acyl	2-Acetyl-3-methylindole	3311	1631
	1 : 2 : 3 : 4-Tetrahydro-1-oxocarbazole	3247	1629

TABLE 3. *Ultraviolet absorption spectra of indolylpyridazinones.*

Compound	$\lambda_{max.}$ (mμ) (log ε)	$\lambda_{min.}$ (mμ) (log ε)
3-3′-Indolylpyridazin-6-one	274 (4·06), 314 (4·34)	245 (3·86), 280 (4·02)
3-(1-Methyl-3-indolyl)pyridazin-6-one	274 (4·02), 322 (4·32)	247 (3·84), 283 (3·87)
3-(5′-Methoxy-1′-methyl-3′-indolyl)pyridazin-6-one	279 (4·21), 326 (4·29), shoulders, 272 (4·15), 313 (4·22)	247 (3·81), 290 (3·88)

EXPERIMENTAL

Unless otherwise stated, the light petroleum used had b. p. 60—80°. Spectroscopic measurements were made as described in Part IV.[1]

3-Acylindoles.—The 3-acetyl, 3-phenylacetyl, and 3-benzoyl derivatives of 2-methylindole were prepared by Seka's method.[3]

3-Acetyl-5-methoxy-2-methylindole was prepared from 5-methoxy-2-methylindole[4] (1·0 g.), with acetonitrile (3 ml.), and hydrogen chloride in ether and subsequent hydrolysis of the resulting ketimine hydrochloride with hot aqueous-alcoholic sulphuric acid. The compound separated from aqueous alcohol in colourless prisms (0·33 g.), m. p. 228—230° (Found: N, 6·9. $C_{12}H_{13}O_2N$ requires N, 6·9%). Similarly prepared, *5-methoxy-2-methyl-3-phenylacetylindole* (yield, 60%) crystallised from benzene in colourless slender needles, m. p. 180—181° (Found: C, 77·2; H, 6·15. $C_{18}H_{17}O_2N$ requires C, 77·4; H, 6·1%), and *3-benzoyl-5-methoxy-2-methylindole* (yield, 50%) from aqueous alcohol in colourless needles, m. p. 171—172° (Found: N, 5·3. $C_{17}H_{15}O_2N$ requires N, 5·3%).

1 : 2 : 3 : 4-Tetrahydro-4-oxocarbazole.—This was best prepared by the method of Clemo and Felton,[5] but was also obtained by cyclisation of *cyclo*hexane-1 : 3-dione monophenylhydrazone with boron trifluoride–ether complex in boiling acetic acid and formed colourless rhombs, m. p. 221°, from aqueous methanol (Found: C, 78·1; H, 5·7; N, 7·5. Calc. for $C_{12}H_{11}ON$: C, 77·8; H, 6·0; N, 7·6%).

1 : 2 : 3 : 4-Tetrahydro-9-methyl-4-oxocarbazole.—The solution obtained by heating *cyclo*hexane-1 : 3-dione *N*-methyl-*N*-phenylhydrazone (5·4 g.) on the steam-bath for 30 min. with concentrated sulphuric acid (20 ml.) and water (50 ml.) was filtered and diluted with water (200 ml.). The resulting *1 : 2 : 3 : 4-tetrahydro-9-methyl-4-oxocarbazole* separated from aqueous acetone in colourless plates (3·0 g.), m. p. 198—199° (Found: C, 78·5; H, 6·6; N, 7·1. $C_{13}H_{13}ON$ requires C, 78·4; H, 6·5; N, 7·0%). This compound was also obtained by the action of methyl sulphate on 1 : 2 : 3 : 4-tetrahydro-4-oxocarbazole dissolved in a mixture of acetone and aqueous potassium hydroxide. The *2 : 4-dinitrophenylhydrazone* crystallised from acetic acid in deep red rectangular prisms, m. p. 297—298° (decomp.) (Found: N, 18·3. $C_{19}H_{17}O_4N_5$ requires N, 18·5%).

[3] Seka, *Ber.*, 1923, **56**, 2058.
[4] Beer, Clarke, Davenport, and Robertson, *J.*, 1951, 2031.
[5] Clemo and Felton, *ibid.*, p. 700.

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2-Acylindoles.—2-Acetyl-3-methylindole was prepared by Oddo's method.[6] 1 : 2 : 3 : 4-Tetrahydro-1-oxocarbazole was prepared by Kent's method [7] and an analogous preparation yielded 1 : 2 : 3 : 4-*tetrahydro*-6-*methoxy*-1-*oxocarbazole* which formed colourless prisms, m. p. 213—214°, from 50% acetone (Found : C, 72·5; H, 5·9; N, 6·8. $C_{13}H_{13}O_2N$ requires C, 72·6; H, 6·0; N, 6·5%). The 2 : 4-*dinitrophenylhydrazone* separated from acetic acid in deep red prisms, m. p. 297° (decomp.) (Found : N, 17·6. $C_{19}H_{17}O_5N_5$ requires N, 17·7%), and the *picrate* crystallised from alcohol in red needles, m. p. 166—167° (Found : C, 51·8; H, 3·6; N, 12·3. $C_{13}H_{13}O_2N,C_6H_3O_7N_3$ requires C, 51·4; H, 3·6; N, 12·6%).

1 : 2 : 3 : 4-*Tetrahydro*-6 : 7-*dimethoxy*-1-*oxocarbazole* formed pale brown needles, m. p. 198°, from alcohol (Found : C, 69·0; H, 5·9; N, 6·0. $C_{14}H_{15}O_3N$ requires C, 68·6; H, 6·1; N, 5·7%) and gave a 2 : 4-*dinitrophenylhydrazone* in dark red prisms, m. p. 293° (decomp.) (from acetic acid) (Found : N, 16·4. $C_{20}H_{19}O_6N_5$ requires N, 16·5%), and a *picrate* in dark red needles, m. p. 193—194° (from alcohol) (Found : C, 50·9; H, 3·4; N, 11·6. $C_{14}H_{15}O_3N,C_6H_3O_7N_3$ requires C, 50·6; H, 3·8; N, 11·8%).

γ-3-Indolyl-γ-oxobutyric Acid.[8]—Indole (17·5 g.), in ether (50 ml.), was added to ethereal ethylmagnesium iodide [from ethyl iodide (23·4 g.) and magnesium (3·6 g.)] at such a rate as to maintain gentle boiling. The mixture was then heated on the steam-bath for 15 min. and diluted with sufficient ether to redissolve the green oil which separated. The solution was decanted from a little residual magnesium and added dropwise during 1 hr. to a stirred solution of β-methoxycarbonylpropionyl chloride [9] (22·5 g.) in ether (40 ml.) at about −10°. The yellow complex was decomposed with ice and ammonium chloride, the ether layer separated, and the aqueous layer extracted with ether (2 × 50 ml.); the combined ether extracts were dried and evaporated. The residual oil was extracted repeatedly with hot light petroleum (b. p. 40—60°) to remove indole, leaving a solid which on crystallisation from benzene–light petroleum gave *methyl γ-3-indolyl-γ-oxobutyrate* in colourless needles (11·0 g.), m. p. 116° (Found : C, 67·2; H, 5·3; N, 5·9. $C_{13}H_{13}O_3N$ requires C, 67·5; H, 5·6; N, 6·1%).

This ester (100 mg.) was heated under reflux with 2N-aqueous sodium hydroxide (7 ml.) until it had dissolved. Acidification of the cooled solution with dilute hydrochloric acid gave γ-3-indolyl-γ-oxobutyric acid, which separated from ethyl acetate in white plates (90 mg.), m. p. 235° (Found : C, 66·2; H, 5·0; N, 6·3. Calc. for $C_{13}H_{11}O_3N$: C, 66·4; H, 5·1; N, 6·1%).

γ-(1-Methyl-3-indolyl)-γ-oxobutyric Acid.—Methyl sulphate (1·5 ml.) was added gradually to an agitated solution of γ-3-indolyl-γ-oxobutyric acid (200 mg.) in acetone (20 ml.) and water (5 ml.), containing potassium hydroxide (1 g.). 15 Min. later the acetone was evaporated, the residual solution acidified with dilute hydrochloric acid, and the precipitate isolated and crystallised from ethyl acetate, giving *γ-(1-methyl-3-indolyl)-γ-oxobutyric acid* in colourless leaflets (190 mg.), m. p. 176° (Found : C, 67·9; H, 5·5; N, 5·8. $C_{13}H_{13}O_3N$ requires C, 67·5; H, 5·6; N, 6·1%). With excess of methyl sulphate, so that the reaction mixture became acid, the major product was the corresponding *methyl ester* which formed colourless needles, m. p. 118°, from benzene–light petroleum (Found : C, 68·9; H, 6·3; N, 5·8. $C_{14}H_{15}O_3N$ requires C, 68·6; H, 6·1; N, 5·7%). On hydrolysis with hot aqueous sodium hydroxide this ester gave γ-(1-methyl-3-indolyl)-γ-oxobutyric acid, m. p. and mixed m. p. 176°.

γ-(5-Methoxy-3-indolyl)-γ-oxobutyric Acid.—Prepared by the method used for the indole derivative, the Grignard compound from 5-methoxyindole [10] (4·0 g.), dissolved in ether–benzene, was added to a solution of β-methoxycarbonylpropionyl chloride (5·6 g.) in ether at −10°. After decomposition of the yellow complex with ice and ammonium chloride, the solid product was collected and recrystallised from methanol, giving *methyl γ-(5-methoxy-3-indolyl)-γ-oxobutyrate* (3·0 g.) in colourless needles, m. p. 188° (Found : C, 64·3; H, 5·8; N, 5·1. $C_{14}H_{15}O_4N$ requires C, 64·4; H, 5·8; N, 5·4%). The ether–benzene layer from the reaction mixture contained only a trace of the ester. Formed in quantitative yield by hydrolysis with 2N-sodium hydroxide, *γ-(5-methoxy-3-indolyl)-γ-oxobutyric acid* separated from acetone–light petroleum in colourless prisms, m. p. 237° (Found : C, 62·6; H, 5·3; N, 5·8. $C_{13}H_{13}O_4N$ requires C, 63·2; H, 5·3; N, 5·7%).

γ-(5-Methoxy-1-methyl-3-indolyl)-γ-oxobutyric Acid.—With methyl sulphate (8 ml.) and

[6] Oddo, *Gazzetta*, 1913, **43**, II, 202.
[7] Kent, *J.*, 1935, 97.
[8] Majima, Shigematsu, and Robkaku, *Ber.*, 1924, **57**, 1453.
[9] *Org. Synth.*, Coll. Vol. III, p. 169.
[10] Blaikie and Perkin, *J.*, 1924, **125**, 296; Hughes and Lions, *J. Proc. Roy. Soc. New South Wales*, 1937—8, **71**, 475.

potassium hydroxide (5 g.) in aqueous acetone methyl γ-(5-methoxy-3-indolyl)-γ-oxobutyrate (1·0 g.) yielded *methyl γ-(5-methoxy-1-methyl-3-indolyl)-γ-oxobutyrate* which crystallised from benzene–light petroleum in colourless prisms (0·8 g.), m. p. 111° (Found : N, 5·1. $C_{15}H_{17}O_4N$ requires N, 5·1%). The corresponding *acid*, obtained as a by-product in this reaction and formed in quantitative yield by alkaline hydrolysis of the ester, separated from ethyl acetate in colourless needles, m. p. 178° (Found : C, 64·1; H, 5·7; N, 5·1. $C_{14}H_{15}O_4N$ requires C, 64·4; H, 5·8; N, 5·4%).

3-3′-*Indolylpyridazin-6-one*.—After concentration, the solution obtained by heating under reflux for 12 hr. methyl γ-3-indolyl-γ-oxobutyrate (1·0 g.), alcohol (15 ml.), and hydrazine hydrate (5 ml.; 98%) deposited the *pyridazinone*. Recrystallised from alcohol, it formed colourless prisms (0·85 g.), m. p. 215° (Found : C, 67·8; H, 5·1; N, 19·5. $C_{12}H_{11}ON_3$ requires C, 67·6; H, 5·2; N, 19·7%).

3-(1-*Methyl-3-indolyl*)*pyridazin-6-one* was similarly prepared from methyl γ-(1-methyl-3-indolyl)-γ-oxobutyrate (0·8 g.) and crystallised from alcohol in pale yellow leaflets (0·7 g.), m. p. 210° (softens 205°) (Found : C, 68·8; H, 5·7; N, 18·4. $C_{13}H_{13}ON_3$ requires C, 68·7; H, 5·7; N, 18·5%).

3-(5-*Methoxy-1-methyl-3-indolyl*)*pyridazin-6-one* (0·45 g.), from methyl γ-(5-methoxy-1-methyl-3-indolyl)-γ-oxobutyrate (0·65 g.) and hydrazine hydrate (3·7 ml.) in alcohol, formed pale yellow prisms, m. p. 232°, from methanol (Found : C, 64·9; H, 5·8; N, 16·6. $C_{14}H_{15}O_2N_3$ requires C, 65·4; H, 5·8; N, 16·3%).

UNIVERSITY OF LIVERPOOL. [*Received, November 26th*, 1956.]

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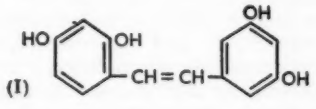
429. 2 : 4 : 3′ : 5′-*Tetrahydroxystilbene from* Artocarpus lakoocha.

By S. MONGOLSUK, ALEXANDER ROBERTSON, and R. TOWERS.

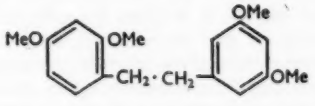
A polyhydric phenol from *Artocarpus lakoocha* has been shown to be 2 : 4 : 3′ : 5′-tetrahydroxystilbene.

CONCENTRATION of a hot aqueous extract of the powdered wood of the Siamese tree *Artocarpus lakoocha* gave a phenolic product from which a tetrahydric phenol with strong reducing properties was isolated as a dihydrate of empirical formula $C_{14}H_{12}O_4,2H_2O$, m. p. 201°, devoid of *C*-methyl or methoxyl group. This unsaturated compound, which formed a tetra-acetate, a tetrabenzoate, and a tetramethyl ether, was shown to contain one ethylene group by perbenzoic acid titration and on hydrogenation furnished a saturated dihydro-derivative which gave a tetra-acetate and a tetramethyl ether. On oxidation with potassium permanganate the tetramethyl ether of the parent phenol yielded a mixture of 2 : 4- and 3 : 5-dimethoxybenzoic acid whilst ozonolysis of the ether produced a mixture of the corresponding aldehydes, separated as their 2 : 4-dinitrophenylhydrazones.

From these results it seemed clear that the compound was 2 : 4 : 3′ : 5′-tetrahydroxystilbene (I) and the synthesis of compound (II), identical with the dihydro-derivative of



(I)



(II)

the stilbene tetramethyl ether, confirmed this. 2 : 4 : 3′ : 5′-Tetrahydroxystilbene has been isolated from the roots of *Neratrum grandiflorum Loes. fil.* by Takaoka [1] who, although he advanced the correct formulation, unfortunately named the stilbene hydroxyresveratrol in spite of the fact that it was devoid of methoxy-group; we consider that this trivial name for the parent stilbene should be abandoned. The annexed Table confirms the identity of the

[1] Takaoka, *J. Chem. Soc. Japan*, 1939, **61**, 96; *J. Fac. Sci., Hokkaido Imp. Univ.*, 1940, III, **3**, 1.

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products from the two sources. Since our work was completed, Barnes and Gerber [2] have reported isolation of the stilbene from *Toxylum pomiferum* wood.

	Takaoka's compound	Phenol from *Artocarpus lakoocha*
Cryst. form	—	Plates
M. p.	199·5°	201°
Ammoniacal $AgNO_3$	Reduces	Reduces
Fehling's soln.	Reduces	Reduces
Tetra-acetate	M. p. 142°	M. p. 142°
Tetra-benzoate	M. p. 193·5°	M. p. 193°
Me_4 ether	Oil	M. p. 84°

Experimental

2 : 4 : 3′ : 5′-*Tetrahydroxystilbene*.—Obtained by concentrating a hot aqueous extract of the powdered wood of *Artocarpus lakoocha*, the light brown powder contained small amounts of resin and gum. The ethereal extract of the crude product was treated with charcoal and evaporated, leaving a brown syrup which slowly crystallised and then on repeated crystallisation from hot water gave the dihydrate of the tetrahydroxystilbene in plates with a transient blue-green ferric reaction in alcohol, m. p. 201°, after softening at about 150° (depending on rate of heating) (Found, in a dried material: C, 60·2; H, 5·9; H_2O, by drying *in vacuo* at 100°, 12·5. Calc. for $C_{14}H_{12}O_4,2H_2O$: C, 59·9; H, 5·8; H_2O, 12·8. Found, in anhyd. compound, m. p. 201° without previous softening: C, 69·2; H, 5·2. Calc. for $C_{14}H_{12}O_4$: C, 68·8; H, 5·0%).

The compound, which readily reduced Fehling's solution and ammoniacal silver nitrate, gave, by the methyl sulphate–potassium carbonate method, a tetramethyl ether forming needles, m. p. 84°, from a little methanol, readily soluble in alcohol or benzene and insoluble in aqueous sodium hydroxide [Found: C, 71·9; H, 6·7; OMe, 39·3%; *M* (Rast), 297. $C_{14}H_8(OMe)_4$ requires C, 72·0; H, 6·7; OMe, 41·3%; *M*, 300]. Prepared by the pyridine– or sodium acetate–acetic anhydride method, the tetra-acetate separated from alcohol in stout needles, m. p. 142° (Found: C, 63·9; H, 4·9; Ac, 40·4. Calc for $C_{14}H_8O_4Ac_4$: C, 64·1; H, 4·9; Ac, 41·8%). With benzoyl chloride and pyridine the phenol gave the tetrabenzoate, prisms, m. p. 193°, from benzene–light petroleum (b. p. 60—80°) and then aqueous acetic acid (Found: C, 75·8; H, 4·2. Calc. for $C_{24}H_{28}O_8$: C, 76·4; H, 4·2%).

***Oxidation of* 2 : 4 : 3′ : 5′-*Tetramethoxystilbene*.**—(*a*) Powdered potassium permanganate (2·0 g.) was added in small portions to an agitated solution of the ether (1 g.) in acetone (100 ml.) and water (5 ml.) and after being kept for 1 hr. the mixture was clarified with sulphur dioxide, acidified with a little dilute sulphuric acid, and concentrated *in vacuo*. After isolation the semisolid was extracted with aqueous sodium hydrogen carbonate, the extract was acidified, and the solid, m. p. 160—177°, was repeatedly crystallised from hot aqueous methanol, giving *O*-dimethyl-α-resorcylic acid, plates, m. p. and mixed m. p. 182° [Found: C, 59·8; H, 5·5; OMe, 34·4. Calc. for $C_7H_4O_2(OMe)_2$: C, 59·3; H, 5·5; OMe, 34·0%]. Evaporation of the aqueous-methanolic mother-liquors followed by extraction with ether gave 2 : 4-dimethoxybenzoic acid, needles, m. p. and mixed m. p. 109°, from dilute methanol and then light petroleum (b. p. 80—100°) (Found: C, 59·8; H, 5·4. Calc. for $C_9H_{10}O_4$: C, 59·3; H, 5·5%).

(*b*) The ozonide from the stilbene tetramethyl ether was decomposed with water, and the product treated with an excess of aqueous 2 : 4-dinitrophenylhydrazine sulphate. The resulting mixture of hydrazones, m. p. 240—248°, which could not be satisfactorily resolved by chromatography on aluminium oxide, was separated by fractionation from warm alcohol. The less soluble product was the 2 : 4-dinitrophenylhydrazone of 3 : 5-dimethoxybenzaldehyde, orange yellow needles, m. p. and mixed m. p. 260—261° (Found: N, 16·2. Calc. for $C_{15}H_{14}O_6N_4$: N, 16·2%). The more soluble fraction consisted of the 2 : 4-dinitrophenylhydrazone of 2 : 4-dimethoxybenzaldehyde, scarlet needles, m. p. and mixed m. p. 258° (Found: N, 15·6%).

1-(2 : 4-*Dihydroxyphenyl*)-2-(3 : 5-*dihydroxyphenyl*)*ethane*.—(*a*) Hydrogenation of 2 : 4 : 3′ : 5′-tetrahydroxystilbene (1 g.) in methanol (100 ml.) with hydrogen and palladium–charcoal gave the *diphenylethane* which separated from water as a *dihydrate* in rectangular plates, m. p. 94—96° (rapid heating) (Found: C, 59·4; H, 6·3; H_2O, 11·5. $C_{14}H_{14}O_4,2H_2O$ requires C, 59·6; H, 6·4; H_2O, 12·8%). On further heating, the compound solidified and then melted at 160°; anhydrous material, m. p. 160°, was also obtained by heating the hydrate *in vacuo* at 80° (Found: C, 68·3; H, 5·8. Calc. for $C_{14}H_{14}O_4$: C, 68·3; H, 5·7%).

[2] Barnes and Gerber, *J. Amer. Chem. Soc.*, 1955, **77**, 3259.

This compound gave a negative ferric reaction in alcohol and a blue reaction in water. Prepared by methyl sulphate–potassium carbonate method, the *tetramethyl ether* separated from 95% methanol (charcoal) in needles, m. p. 51—52° [Found: C, 71·4; H, 7·0; OMe, 40·6. $C_{14}H_{10}(OMe)_4$ requires C, 71·5; H, 7·5; OMe, 41·0%]. The *tetra-acetate* formed needles, m. p. 75°, identical with a specimen obtained by the hydrogenation of 2 : 4 : 3′ : 5′-tetra-acetoxystilbene (Found: C, 64·2; H, 5·3. $C_{22}H_{22}O_8$ requires C, 63·8; H, 5·4%).

(*b*) 3 : 5-Dimethoxybenzyl cyanide (1·75 g.) was condensed with resorcinol (1·1 g.) in ether (75 ml.) by zinc chloride (1 g.) and an excess of hydrogen chloride, and the ketimine washed with much ether and hydrolysed with hot water. A solution of the resulting oil in ether (150 ml.) was washed with aqueous sodium hydrogen carbonate (10 ml. × 3) to remove traces of acidic material and then extracted with 2% aqueous sodium hydroxide. Acidification of the extracts gave ω-(3 : 5-*dimethoxyphenyl*)*resacetophenone*, which separated from dilute methanol in rhombs (0·6 g.), m. p. 137°, with a red-brown ferric reaction [Found: C, 66·7; H, 5·2; OMe, 21·3. $C_{14}H_{10}O_3(OMe)_2$ requires C, 66·7; H, 5·6; OMe, 21·5%]. By the methyl sulphate–potassium carbonate method this was converted into 3 : 5-*dimethoxybenzyl* 2 : 4-*dimethoxyphenyl ketone*, m. p. 107° after purification from methanol (Found: C, 68·4; H, 6·4. $C_{18}H_{20}O_5$ requires C, 68·4; H, 6·4%).

Reduction of this ketone by Clemmensen's method furnished the diphenylmethane in needles, m. p. 50°, undepressed on admixture with a "natural" specimen, m. p. 51—52° (Found: C, 71·4; H, 7·5. Calc. for $C_{18}H_{22}O_4$: C, 71·5; H, 7·3%).

In attempts to synthesise the tetramethyl ether of the hydroxystilbene, α-(3 : 5-dimethoxyphenyl)-2 : 4-dimethoxycinnamonitrile was prepared by the condensation of 2 : 4-dimethoxybenzaldehyde (1 g.) and 3 : 5-dimethoxybenzyl cyanide [2] (1 g.) in alcohol (250 ml.) with sodium ethoxide (5 ml. of 5% alcoholic solution) at room temperature for 1 hr. In almost quantitative yield this *nitrile* crystallised from alcohol in yellow needles, m. p. 120° (Found: C, 69·6; H, 5·8; N, 4·4. $C_{19}H_{19}O_4N$ requires C, 70·1; H, 5·8; N, 4·3%). Attempts to hydrolyse this compound with acidic or alkaline reagent gave intractable products.

UNIVERSITY OF LIVERPOOL. [*Received, December 6th*, 1956.]

Adams, McKenzie, and Lowe, *ibid.*, 1948, **70**, 664.

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430. *Diospyrol, a Constituent of* Diospyros mollis.

By J. W. LODER, S. MONGOLSUK, ALEXANDER ROBERTSON, and W. B. WHALLEY.

The principal constituent of the fruit of *Diospyros mollis* is a 2 : 2′-dinaphthyl, closely related to gossypol.

THE crude extract of the fruit of the shrub, *Diospyros mollis*, which is used in Far Eastern countries as an anthelmintic, has been examined and the principal component appears to be a readily oxidisable, new, tetrahydric phenol, diospyrol, $C_{22}H_{18}O_4$, which is devoid of methoxyl groups, contains two *C*-methyl groups, and gives a tetra-acetate. On methylation diospyrol furnishes tetra-*O*-methyldiospyrol, the general properties and infrared spectrum of which confirm the absence of additional hydroxyl or carbonyl functions. Oxidation of tetra-*O*-methyldiospyrol gives a di-*p*-quinone, di-*O*-methyldiospyroquinone, $C_{22}H_{12}O_4(OMe)_2$, which is converted by reductive acetylation into tetra-*O*-acetyl-di-*O*-methyldiospyroquinol, $C_{22}H_{12}(OAc)_4(OMe)_2$. These results, in conjunction with the spectral data, indicate a dinaphthyl type of structure for diospyrol. From an inspection of the ultraviolet absorption spectra of diospyrol and its derivatives (Table 1) together with those of various 2 : 2′-dinaphthyls (Table 2) and of deoxygossypol derivatives,[1,2] it seems reasonably certain that diospyrol contains a 2 : 2′-dinaphthyl

[1] Shirley and Sheehan, *J. Amer. Chem. Soc.*, 1955, **77**, 4606.
[2] Shirley and Dean, *ibid.*, p. 6077.

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chromophore. Furthermore, a comparison of the ultraviolet absorption spectra of tetra-*O*-methyldiospyrol, 1 : 1′-dimethoxy-2 : 2′-dinaphthyl, and 4 : 8 : 4′ : 8′-tetramethoxy-3 : 3′-dimethyl-2 : 2′-dinaphthyl indicates the possible presence of a 1 : 1′-dihydroxy-2 : 2′-dinaphthyl nucleus in diospyrol.

TABLE 1. *Absorption spectra of diospyrol derivatives.*[a]

Substance	$\lambda_{max.}$ (mμ)	log ε	$\lambda_{min.}$ (mμ)	log ε
Tetra-*O*-methyldiospyrol	225	4·64	228	4·63
	242	4·88		
	ca. 256[b]	*ca.* 4·71	281	4·09
	300—340[c]	*ca.* 4·2		
Tetra-*O*-acetyldiospyrol	221	4·76	225	4·74
	237	4·99		
	250[b]	4·81		
	ca. 290[b]	*ca.* 4·1		
Tetra-*O*-acetyldi-*O*-methyldiospyroquinol	218	4·73	229	4·63
	239	4·82	248	4·66
	261	4·79		
	ca. 300[b]	*ca.* 4·15		
Di-*O*-methyldiospyroquinone[d]	—	—	238	4·43
	256	4·52		
	375	3·94	311	3·46

[a] Results were obtained in 95% ethanol on a Unicam Model S.P. 500 Quartz Spectrophotometer. [b] Shoulder. [c] Ill-defined fine structure. [d] In dioxan.

TABLE 2. *Absorption spectra of some dinaphthyls.*[a]

Substance	$\lambda_{max.}$ (mμ)	log ε	$\lambda_{min.}$ (mμ)	log ε
2 : 2′-Dimethoxy-1 : 1′-dinaphthyl[e]	230	4·95	254	3·62
	282	3·91	291	3·86
	294	3·87	314	3·49
	326	3·68	330	3·67
	340	3·76		
1 : 1′-Dimethoxy-2 : 2′-dinaphthyl	218	4·74	227	4·64
	236	4·72	243	3·68
	257	4·81		
	ca. 292[b]	*ca.* 4·14		
4 : 8 : 4′ : 8′-Tetramethoxy-3 : 3′-dimethyl-2 : 2′-dinaphthyl	224	4·84	230	4·83
	243	4·95	283	4·11
	289	4·14	294	4·14
	301	4·17	312	4·04
	315	4·06	326	3·80
	330	3·89		
1 : 4 : 1′ : 4′-Tetra-acetoxy-2 : 2′-dinaphthyl[f]	217	4·75	225	4·67
	235	4·82		
	ca. 247[b]	*ca.* 4·77		
	ca. 286[b,c]	*ca.* 4·18		
2 : 2′-Di-1 : 4-Naphthaquinone[d,h]	246	4·49	226	4·33
	266	4·45	260	4·43
	337	3·79	315	3·74
	428	2·87	396	2·75

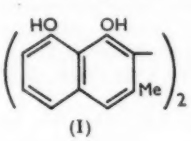
[a–d] See Table 1. [e] Ostermayer and Rosenhek, *Ber.*, 1884, **17**, 2453. [f] Clemo, Cockburn, and Spence, *J.*, 1931, 1265. [g] Rosenhauer, Braun, Pummerer, and Riegelbauer, *Ber.*, 1937, **70**, 2281. [h] Ullmann, *Helv. Chim. Acta*, 1926, **9**, 442.

This concept is compatible with the fact that the strongest band in the ultraviolet spectra of the diospyrol derivatives (λ 237—242 mμ; log ε *ca.* 4·9) and of 1 : 1′-disubstituted 2 : 2′-dinaphthyls (λ 235—243 mμ; log ε *ca.* 4·8) is at a shorter wavelength than that of 2 : 2′-dinaphthyl (λ 245 mμ; log ε 5·0). The hypsochromic shift is due to hindered rotation, attributable to substituents in the 1- and/or 3-position, preventing a completely planar structure.[3,4] Current theories of plant product biogenesis,[5] in conjunction with

[3] Friedel, Orchin, and Reggel, *J. Amer. Chem. Soc.*, 1948, **70**, 199.
[4] Edwards and Cashaw, *ibid.*, 1954, **76**, 6141.
[5] Birch and Donovan, *Chem. and Ind.*, 1954, **32**, 1047.

the isolation [6,7,8,9] of plumbagin (VII) from various species of *Diospyros* and of the phenol (VIII) from *D. hebecarpa* [6] and other general considerations, provide collateral biogenetic evidence in support of the proposed symmetrical structure for diospyrol, for the location of hydroxyl groups in the 1 : 1′-positions, and for the 3 : 3′-methyl groups, which from the spectral data for gossypol, should produce no further hypsochromic effects on the spectrum. These desiderata, in conjunction with the green ferric reaction of diospyrol, indicate a structure (I), although alternative formulations, *e.g.*, (II), cannot be excluded.

Confirmation of structure (I) for diospyrol was sought by an unequivocal synthesis of 4 : 8 : 4′ : 8′-tetramethoxy-3 : 3′-dimethyl-2 : 2-dinaphthyl (VI), an isomer of tetra-*O*-methyldiospyrol, which it was hoped would afford di-*O*-methyldiospyroquinone (III) on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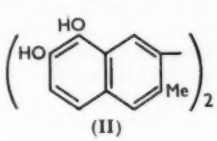
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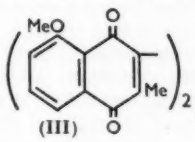
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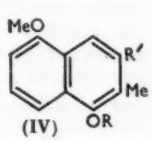
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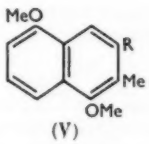
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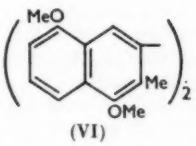
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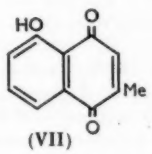
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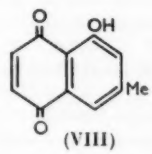
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oxidation. The Stobbe condensation of *o*-methoxybenzaldehyde with ethyl methylsuccinate followed by cyclisation [10] of the product gave the acetoxynaphthoate (IV; R = Ac, R′ = CO_2Et), which was then converted by the stages (IV; R = H, R′ = CO_2H), (IV; R = Me, R′ = CO_2Me), (IV; R = Me, R′ = $CO{\cdot}NH{\cdot}NH_2$), (V; R = NH_2), and (V; R = I) into the desired 2 : 2′-dinaphthyl (VI), according to standard methods. Unfortunately, repeated attempts to obtain a crystalline quinone from (VI) with chromic oxide, hydrogen peroxide, lead tetra-acetate, or periodic acid were unsuccessful.

Experimental

Tetra-O-methyldiospyrol.—When the dried, crushed, ripe fruit of *Diospyros mollis* (10 kg.) was extracted continuously with ether, the crude phenol (70—90 g.) gradually separated from the ethereal solution as a grey powder, which gave an intense green ferric reaction in alcohol and was extremely sensitive to aerial oxidation, especially in solution. Repeated crystallisation of the product from methanol (charcoal) furnished *diospyrol* in needles, m. p. 251—257° (decomp.), which darkened rapidly in air and had an intense green ferric reaction in alcohol (Found: C, 76·8; H, 5·4; *C*-Me, 8·7. $C_{20}H_{12}O_4Me_2$ requires C, 76·3; H, 5·2; *C*-Me, 8·0%). Material sufficiently pure for methylation and acetylation was obtained when a slurry of the crude phenol (1 part) in methanol (5 parts) was rapidly heated to the b. p. and filtered and the residue washed with hot methanol (5 parts). A mixture of this product (8 g.), potassium carbonate (25 g.), methyl sulphate (16 g.), and acetone (200 ml.) was heated under reflux in nitrogen for 10 hr. A solution of the methylation product in benzene was treated with charcoal and filtered and the yellow fluorescent filtrate chromatographed on aluminium oxide. Purification of the eluate from benzene gave *tetra*-O-*methyldiospyrol* (3·1 g.) in tablets, m. p. 232°, unchanged by sublimation at 250°/0·01 mm. [Found: C, 77·4, 77·7; H, 6·7, 6·9; OMe, 30·3, 30·2; *C*-Me, 6·5, 6·5%; *M* (ebullioscopic in benzene) 397, 412. $C_{20}H_8Me_2(OMe)_4$ requires C, 77·6; H, 6·5; OMe, 30·9; *C*-Me, 7·5%; *M*, 402]. This ether was sparingly soluble in the usual organic solvents and devoid of a ferric reaction in alcohol.

[6] Cooke and Dowd, *Austral. J. Sci. Res.*, 1952, **5**, *A*, 760.
[7] Meijer, *Rec. Trav. chim.*, 1947, **66**, 193.
[8] Paris and Moyse-Mignon, *Compt. rend.*, 1949, **228**, 2063.
[9] Paris and Prista, *Ann. Pharm. franç.*, 1954, **12**, 375.
[10] Borsche, *Annalen*, 1936, **526**, 1.

Tetra-O-*acetyldiospyrol*.—A solution of partially purified diospyrol (5 g.) in acetic anhydride (50 ml.), containing sodium acetate (8 g.), was refluxed for 1 hr. and then poured on ice. Next day the precipitate was purified from methanol, chromatographed on aluminium oxide from a solution in benzene, and then sublimed at 240°/0·01 mm., giving *tetra*-O-*acetyldiospyrol* (1·7 g.) which separated from benzene–ethanol in prisms, m. p. 233°, devoid of a ferric reaction; with tetra-*O*-methyldiospyrol it melted at *ca.* 208—225° (Found: C, 69·8, 70·4; H, 5·2, 5·1. $C_{30}H_{26}O_8$ requires C, 70·0; H, 5·1%).

Tetrabromotetra-O-*methyldiospyrol*.—Prepared by adding an excess of bromine in chloroform to a solution of tetra-*O*-methyldiospyrol (250 mg.) in chloroform, *tetrabromotetra*-O-*methyldiospyrol* (85 mg.) separated from benzene in needles, m. p. 310° (Found: C, 43·1; H, 2·9; Br, 48·2. $C_{26}H_{22}O_4Br_4$ requires C, 43·5; H, 3·1; Br, 44·4%).

Di-O-*methyldiospyroquinone*.—Hydrogen peroxide (12 ml.; 100-vol.) was added during 15 min. to a boiling solution of tetra-*O*-methyldiospyrol (2 g.) in acetic acid (80 ml.), followed by water (80 ml.), and the solution boiled for a further 15 min., a crystalline product separating. Purification of this from acetic acid and then toluene gave *di*-O-*methyldiospyroquinone* (0·27 g.) in dark red prisms, m. p. 250° (decomp.) [Found: C, 71·7, 71·6; H, 4·7, 4·7; OMe, 14·9; *C*-Me, 6·7, 7·0. $C_{20}H_6O_4Me_2(OMe)_2$ requires C, 71·6; H, 4·5; OMe, 15·5; *C*-Me, 7·5%].

Reductive acetylation of this quinone (170 mg.) in boiling acetic anhydride (10 ml.), containing sodium acetate (0·2 g.) and zinc dust (0·1 g.), for ½ hr. gave *tetra*-O-*acetyldi*-O-*methyldiospyroquinol* (120 mg.) which separated from methanol in almost colourless prisms, m. p. 242° [Found: C, 66·7; H, 5·3; OMe, 10·9%; *M* (*X*-ray crystallographic), 562. $C_{30}H_{24}O_8(OMe)_2$ requires C, 66·9; H, 5·3; OMe, 10·8%; *M*, 575].

4 : 8 : 4′ : 8′-*Tetramethoxy*-3 : 3′-*dimethyl*-2 : 2′-*dinaphthyl*.—To a well-stirred mixture of sodium hydride (25 g.) and benzene (500 ml.) in nitrogen, ethanol (5 ml.) was added, followed dropwise by a solution of *o*-methoxybenzaldehyde (57 g.) in ethyl methylsuccinate (200 ml.), at a rate sufficient to maintain a steady evolution of hydrogen and a temperature of 40°. The mixture was then stirred for 1 hr. and acetic acid (100 ml.) was cautiously added, followed by water (200 ml.). An ethereal solution of the product was repeatedly washed with an excess of 2N-aqueous sodium carbonate, and the combined washings were acidified and extracted with ether. Evaporation of the dried extracts gave ethyl hydrogen β-2-methoxybenzylidene-α-methylsuccinate (77 g.) as an oil which was cyclised with boiling acetic anhydride (140 ml.) and sodium acetate (21 g.) during 5 hr. The mixture was poured on ice and next day the dark oil which had separated was repeatedly extracted with boiling light petroleum (b. p. 60—80°). The residue left on evaporation of the combined extracts was purified from ethanol (100 ml.), giving *ethyl* 4-*acetoxy*-8-*methoxy*-3-*methyl*-2-*naphthoate* which formed needles (17 g.), m. p. 112°, from methanol or light petroleum (b. p. 60—80°) (Found: C, 67·6; H, 6·1. $C_{17}H_{18}O_5$ requires C 67·5; H, 6·0%). Hydrolysis of this ester (16 g.) with boiling 10% aqueous–alcoholic sodium hydroxide for 5 hr. gave 4-*hydroxy*-8-*methoxy*-3-*methyl*-2-*naphthoic acid* (12 g.) which separated from acetic acid in needles, m. p. 244° (Found: C, 67·1; H, 5·3; OMe, 13·4. $C_{12}H_9O_3{\cdot}OMe$ requires C, 67·2; H, 5·2; OMe, 13·4%).

Methylation of this phenolic acid (13 g.) in boiling acetone (200 ml.) with methyl iodide (20 ml.) and potassium carbonate (10 g.) for 9 hr. furnished *methyl* 4 : 8-*dimethoxy*-3-*methyl*-2-*naphthoate* (12 g.), forming yellow prisms, m. p. 110°, from light petroleum (b. p. 60—80°) [Found: C, 68·9; H, 6·4; OMe, 35·7. $C_{12}H_7O(OMe)_3$ requires C, 69·2; H, 6·2; OMe, 35·8%]. A solution of this ester (1 g.) in ethanol (10 ml.), containing hydrazine hydrate (2 ml.), was refluxed for 7 hr. and evaporated to a small volume. The resulting *hydrazide* was recrystallised from ethanol, forming needles, m. p. 211° (Found: C, 64·2; H, 5·8; N, 10·8. $C_{14}H_{16}O_3N_2$ requires C, 64·6; H, 6·2; N, 10·8%).

A solution of this hydrazide (11·2 g.) in hot alcohol (500 ml.) was cooled until crystallisation began, and then treated with ethanolic hydrogen chloride (16 ml., containing 2·3 g. of hydrogen chloride) followed by ethyl nitrite (4 g.) in alcohol (10 ml.). The mixture was kept for 15 hr. at 0°, 1 hr. at room temperature, and 1 hr. at 100°, the greater part of the solvent was then distilled off, and the residue mixed with 20% methanolic potassium hydroxide (250 ml.), boiled for ½ hr., cooled, and extracted with benzene. The benzene extract was washed with warm 2N-hydrochloric acid, and the amine precipitated from the acidic extract with ammonia (*d* 0·88) at 0°. Purification from light petroleum (b. p. 60—80°) followed by vacuum-sublimation gave 4 : 8-*dimethoxy*-3-*methyl*-2-*naphthylamine* in needles (5·7 g.), m. p. 90° (Found: C, 71·9; H, 6·6. $C_{13}H_{13}O_2N$ requires C, 71·9; H, 7·0%).

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A solution of this amine (5·3 g.) in water (70 ml.) and concentrated sulphuric acid (10·5 ml.) was diazotised at 0° with sodium nitrite (2 g.) in water (20 ml.), and 1½ hr. later the mixture was treated with potassium iodide (11 g.) in water (10 ml.), kept for 1½ hr., and heated on the steam-bath for 30 min. The product, isolated with light petroleum (b. p. 60—80°) and purified by chromatography on aluminium oxide followed by crystallisation from aqueous alcohol, gave *3-iodo-1 : 5-dimethoxy-2-methylnaphthalene* in needles (7·6 g.), m. p. 98° (Found : C, 47·8; H, 4·0. $C_{13}H_{13}O_2I$ requires C, 47·6; H, 4·0%).

A mixture of the iodonaphthalene (7·5 g.), copper bronze (5 g.), and a crystal of iodine was heated at 210° for 5 hr., and the cooled, crushed product exhaustively extracted with light petroleum (b. p. 60—80°). The extract was chromatographed on aluminium oxide from benzene to give *4 : 8 : 4′ : 8′-tetramethoxy-3 : 3′-dimethyl-2 : 2′-dinaphthyl* which separated from methanol in prisms (2·1 g.), m. p. 176° [Found : C, 77·6; H, 6·8; OMe, 31·2. $C_{22}H_{14}(OMe)_4$ requires C, 77·6; H, 6·5; OMe, 30·8%].

We thank Dr. G. E. Little for assistance with the preparation of tetra-*O*-methyldiospyrol. The analyses were performed by Mr. A. S. Inglis, M.Sc., and his associates of this Department.

UNIVERSITY OF LIVERPOOL. [*Received, December 6th*, 1956.]

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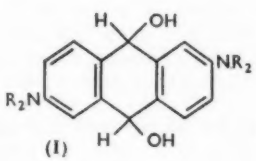
431. *The Action of Tin and Hydrochloric Acid on* p-*Dialkylaminobenzaldehydes. Part II.* The Preparation of Some New Anthracenes.*

By JACK W. RASBURN and FREDERICK H. C. STEWART.

The reaction of *p*-dialkylaminobenzaldehydes with tin and hydrochloric acid to give 2 : 6-bisdialkylaminoanthracenes has been extended to include several 2-substituted *p*-dimethylaminobenzaldehydes. Certain steric aspects of the reaction are also discussed.

IN Part I it was shown that *p*-dialkylaminobenzaldehydes react with tin and hydrochloric acid to form 2 : 6-bisdialkylamino-9 : 10-dihydro-9 : 10-dihydroxyanthracenes (I) which are then reduced by the stannous chloride present to 2 : 6-bisdialkylaminoanthracenes. The behaviour of a diol (I) depends markedly on the nature of the dialkylamino-group. Thus



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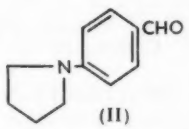

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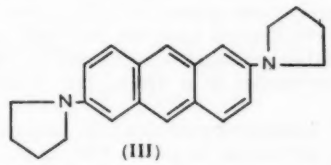

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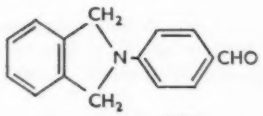

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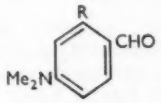

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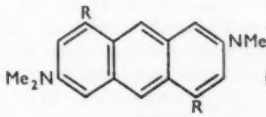

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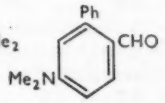

(VII)

the diethylamino-compound (I; R = Et) was less readily reduced than the dimethylamino-analogue (I; R = Me). This effect, which was ascribed to steric inhibition of resonance in the former diol, has now been examined further in the case of 1-*p*-formylphenylpyrrolidine (II) in which steric interference between the dialkylamino-group and the

* Part I, Stewart, *J.*, 1957, 1026.

aromatic nucleus should be reduced owing to the rigidity imposed by the heterocyclic ring. In fact, the aldehyde (II) reacted readily with tin and hydrochloric acid to give 2 : 6-dipyrrolidinoanthracene (III) in 57% yield. Under the same conditions *p*-diethylaminobenzaldehyde gave only a trace of 2 : 6-bisdiethylaminoanthracene, the main product being unreduced diol (I; R = Et), while *p*-dimethylaminobenzaldehyde gave 2 : 6-bisdimethylaminoanthracene in some 35% yield. An attempt to apply the reaction to 2-*p*-formylphenyl*iso*indoline (IV) was unsuccessful owing to its very low solubility.

While it is thus clear that the reaction is very sensitive to relatively minor steric effects at the dialkylamino-group nothing is known regarding similar influences at the aldehyde function. Consequently, the effect of various substituents *ortho* to the aldehyde group in *p*-dimethylaminobenzaldehyde has now been investigated.

The aldehydes (V; R = Me, OMe, Cl) react readily with tin and hydrochloric acid, to give the corresponding anthracenes (VI; R = Me, OMe, Cl) in yields of 40—55%. These results indicate that the reaction is virtually unaffected by moderate steric hindrance at the aldehyde group. A particularly interesting compound in this connection is 4-dimethylamino-2-phenylbenzaldehyde (VII). With this aldehyde intramolecular condensation at the 2′-position to form a fluorene derivative was a possible mode of reaction. The steric effect of the bulky phenyl group might also be expected to facilitate such condensation rather than the alternative intermolecular diol-forming reaction. However, the aldehyde (VII) gave 2 : 6-bisdimethylamino-4 : 8-diphenylanthracene in 37% yield. There was no indication of the simultaneous formation of a fluorene derivative.

The mechanism and applications of this reaction are being further investigated.

Experimental

Preparation of p-*Dialkylaminobenzaldehydes.*—The aldehydes were prepared from the dialkylanilines by the *NN*-dimethylformamide–phosphorus oxychloride procedure of Campaigne and Archer.[1] The mixture was poured with stirring into a large excess of cold water; the product separated slowly. Neutralization with sodium acetate [1] was found to be unnecessary in most cases and tended to yield an inferior product.

The substituted dimethylanilines which were required were prepared by the trimethyl phosphate method of Thomas, Billman, and Davies [2] which was found to be more uniformly satisfactory than the various methods described elsewhere.

The following aldehydes are new.

2-p-*Formylphenyliso*indoline (IV), obtained from 2-phenyl*iso*indoline [3] as a buff powder after recrystallisation from benzene–light petroleum (b. p. 60—80°), had m. p. 176—177° (70%). When sublimed *in vacuo* and recrystallised from benzene–light petroleum, it formed light yellow needles, m. p. 176·5—177° (Found: C, 80·9; H, 5·7. $C_{15}H_{13}ON$ requires C, 80·7; H, 5·8%).

1-p-*Formylphenylpyrrolidine* (II), prepared (69%) from 1-phenylpyrrolidine,[4] recrystallised from light petroleum (b. p. 80—100°) in plates, m. p. 84·5—85·5° (Found: C, 75·3; H, 7·05; N, 8·2. $C_{11}H_{13}ON$ requires C, 75·4; H, 7·5; N, 8·0%).

4-*Dimethylamino*-2-*phenylbenzaldehyde* (VII), prepared (50%) from 3-dimethylaminodiphenyl,[5] formed a white powder which was sufficiently pure for further use (m. p. 55—56°). It recrystallised from light petroleum (b. p. 60—80°) in plates, m. p. 55—56° (Found: C, 80·2; H, 6·7; N, 6·2. $C_{15}H_{15}ON$ requires C, 80·0; H, 6·6; N, 6·2%).

4-*Dimethylamino*-2-*methoxybenzaldehyde* (V; R = OMe), obtained from *NN*-dimethyl-*m*-anisidine [6] and purified by distillation, had b. p. 190—192°/7 mm., m. p. 58—60° (48%), and recrystallised from light petroleum (b. p. 60—80°) in needles, m. p. 61—62° (Found: C, 67·0;

[1] Campaigne and Archer, *J. Amer. Chem. Soc.*, 1953, **75**, 989.
[2] Thomas, Billman, and Davies, *ibid.*, 1946, **68**, 895.
[3] Scholtz, *Ber.*, 1898, **31**, 628.
[4] Sommers, *J. Amer. Chem. Soc.*, 1956, **78**, 2439.
[5] Groenewoud and Robinson, *J.*, 1934, 1692.
[6] Reverdin and Luc, *Ber.*, 1914, **47**, 1541.

H, 7·5; N, 7·9. $C_{10}H_{13}O_2N$ requires C, 67·0; H, 7·3; N, 7·8%). The *semicarbazone* formed needles (from ethanol), m. p. 234—235° (Found: C, 55·9; H, 6·7; N, 23·6. $C_{11}H_{16}O_2N_4$ requires C, 55·9; H, 6·8; N, 23·7%). The monoaldehyde was accompanied by higher-melting colourless needles (from ethanol), m. p. 157—158° (16%), probably 4-*dimethylamino*-6-*methoxy*-iso*phthaldehyde* (Found: C, 63·45; H, 6·4; N, 6·8. $C_{11}H_{13}O_2N$ requires C, 63·75; H, 6·3; N, 6·8%).

Preparation of 2 : 6-*Bisdialkylaminoanthracenes.*—The general procedure was that described in Part I. The *p*-dialkylaminobenzaldehyde (1 part) was dissolved in diluted hydrochloric acid (60 parts; 1 : 1 v/v), and granulated tin (4 parts) added. The mixture was kept at 20—30° until most of the metal had dissolved (1—2 weeks). The precipitated tin salt was then separated and treated with alkali to liberate the crude anthracene, which was dried and recrystallised from an appropriate solvent. In this manner the following 2 : 6-bisdialkylaminoanthracenes were prepared.

2 : 6-*Bisdimethylamino*-4 : 8-*dimethylanthracene* (VI; R = Me), from 4-dimethylamino-2-methylbenzaldehyde,[7] formed golden-yellow needles [from benzene–ethanol (1 : 2)], m. p. 175—176° (39%) (Found: C, 81·4; H, 8·7; N, 9·4. $C_{20}H_{24}N_2$ requires C, 82·1; H, 8·2; N, 9·5%).

4 : 8-*Dichloro*-2 : 6-*bisdimethylaminoanthracene* (VI; R = Cl) (48%), from 2-chloro-4-dimethylaminobenzaldehyde,[8] recrystallised from benzene (charcoal) in yellow elongated plates (opaque on storage), m. p. 205·5—206·5° (Found: C, 64·8; H, 5·7. $C_{18}H_{18}N_2Cl_2$ requires C, 64·9; H, 5·4%).

2 : 6-*Bisdimethylamino*-4 : 8-*dimethoxyanthracene* (VI; R = OMe) (55%), from 4-dimethylamino-2-methoxybenzaldehyde, crystallised in yellow needles [from benzene–ethanol (1 : 2)], m. p. 206—207° (Found: C, 73·8; H, 6·9; N, 8·7. $C_{20}H_{24}O_2N_2$ requires C, 74·0; H, 7·5; N, 8·6%).

2 : 6-*Bisdimethylamino*-4 : 8-*diphenylanthracene* (VI; R = Ph) (37%), from 4-dimethylamino-2-phenylbenzaldehyde (VII), formed pale yellow needles, m. p. 173·5—174·5°, from benzene–ethanol (charcoal) (Found: C, 86·4; H, 6·8; N, 6·6. $C_{30}H_{28}N_2$ requires C, 86·5; H, 6·8; N, 6·7%).

2 : 6-*Dipyrrolidinoanthracene* (III), from 1-*p*-formylphenylpyrrolidine (II), formed light yellow needles, m. p. 315—318° (57%), from boiling benzene (in which it was rather sparingly soluble). Recrystallised from benzene (charcoal) it had m. p. 315—317° (Found: C, 83·1; H, 7·95; N, 8·95. $C_{22}H_{24}N_2$ requires C, 83·5; H, 7·65; N, 8·85%).

Solutions of these anthracenes exhibited a strong blue fluorescence. Treatment of each with hydrogen peroxide and hydrochloric acid under the conditions described in Part I produced a thermolabile red colour. This reaction appears to be characteristic of 2 : 6-bisdialkylaminoanthracenes.

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[*Received, January 4th,* 1957.]

[7] Duff, *J.*, 1945, 276.
[8] Ullmann and Frey, *Ber.*, 1904, **37**, 864.

XUM

432. *Dithiols. Part XIX.* Further Studies on the Deacetylation of Acetylated Dithiols.*

By Peter S. Fitt and L. N. Owen.

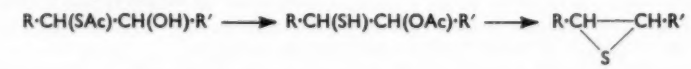
4 : 5-Dimercaptopentanol and its triacetyl, di-*S*-acetyl, and *O*-acetyl derivatives have been synthesised; alkaline hydrolysis of these acetates, unlike that of the 3 : 4-dimercaptobutanol derivatives, proceeds without cyclisation, though there is evidence of acetyl migration in the bisthiolacetate. Attempts to prepare 3 : 4-bisacetylthiopentyl acetate, by addition of thiolacetic acid to pent-3-yn-1-yl acetate, gave only the mono-adduct, 3-acetylthiopent-3-en-1-yl acetate, the light absorption of which is anomalous.

Toluene-*p*-sulphonyl derivatives of mono-*O*-*iso*propylidenepentaerythritol show very low reactivity in substitution reactions, probably because of the *neo*pentyl type of structure.

The two stereoisomeric forms of 2 : 3-dimercaptobutane-1 : 4-diol, and several derivatives, have now been synthesised; alkaline deacetylation of the acetyl derivatives is accompanied by cyclisation.

Unlike 2 : 3-bisacetylthiopropyl acetate, which on mild alkaline hydrolysis readily gives 3-acetylthiopropylene sulphide, 2-acetoxy-1 : 3-bisacetylthiopropane undergoes little or no cyclisation. The absence of cyclisation in the alkaline hydrolysis of a series of αω-bisthiolacetates shows that there is no tendency for alkyl–sulphur fission in the thiolacetate group.

Previous investigations [1,2] have revealed that alkaline hydrolysis of certain acetylated vicinal hydroxy-thiols gives the episulphide in addition to the free hydroxy-thiol, and that similar results are obtained with the partly acetylated derivatives. The *S*-acetyl compound also underwent preliminary isomerisation into the *O*-acetate, the latter being the actual precursor of the episulphide :



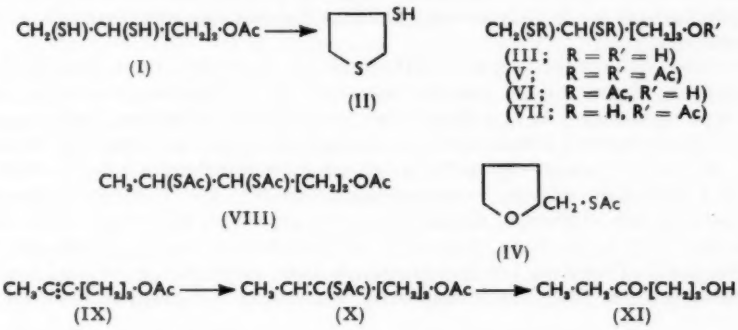
Similar treatment of the mono- or the di-acetyl derivatives of 3-mercaptopropanol, 3-mercaptobutanol, and 4-mercaptobutanol showed [3] that in these non-vicinal structures cyclisation to four- or five-membered ring sulphides did not occur; acetyl migration was observed, however, with the *S*-acetyl derivative of 3-mercaptopropanol and of 3-mercaptobutanol, but not with that of 4-mercaptobutanol, which indicated that a six-membered orthoacetate ring intermediate represented the limiting size for this isomerisation. The absence of cyclisation was interesting in view of the fact that alkaline hydrolysis of the fully or partly acetylated derivatives of 3 : 4-dimercaptobutanol [*e.g.*, (I)] had been shown [1,2] to give 3-mercaptothiophan (II), and it was therefore clear that cyclisation in the latter instance was facilitated by the presence of the additional thiol group. Two possible reasons were suggested, one involving direct activation of one thiol group by its neighbour, and the other the formation of a chelate ring. If the first suggestion were correct, the acetyl derivatives (or at least the *O*-acetate) of 4 : 5-dimercaptopentanol (III) should also be capable of undergoing cyclisation to give either 2-mercaptomethylthiophan or tetrahydro-3-mercaptothiopyran, and the synthesis of the pentanol (III) was therefore investigated.

Reaction of 4 : 5-dibromopentanol with potassium thiolacetate failed to give any pure 4 : 5-bisthiolacetate, the main identifiable product being tetrahydrofurfuryl thiolacetate

* Part XVIII, Johary and Owen, *J.*, 1955, 1307.

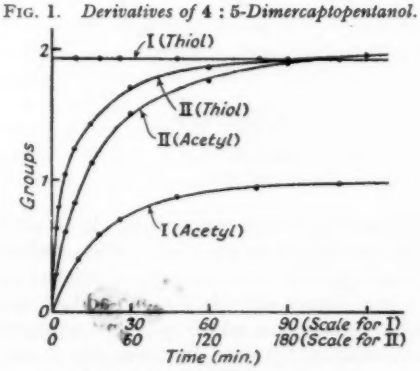
[1] Miles and Owen, *J.*, 1952, 817.
[2] Harding and Owen, *J.*, 1954, 1528.
[3] *Idem, ibid.*, p. 1536.

(IV), evidently formed by intramolecular elimination of hydrogen bromide from the secondary position. To obviate this difficulty, 4 : 5-dibromopentyl acetate was used instead of the dibromo-alcohol, and 4 : 5-bisacetylthiopentyl acetate (V) was obtained in good yield. Quantitative alkaline hydrolysis of this showed that no cyclisation occurred,



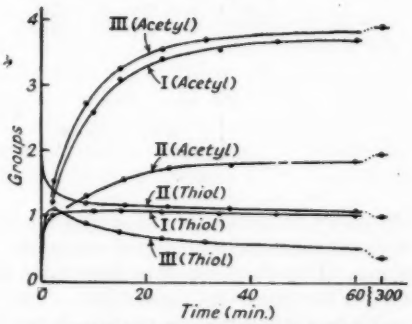
the final thiol value corresponding to that for completely normal hydrolysis, but this result was not conclusive because it was conceivable that the *O*-acetyl group was undergoing preferential hydrolysis to give the di-*S*-acetyl compound (VI); since cyclisation involves attack by a free thiol group (as anion) on the *O*-acetate, this clearly could not take place unless preceded by acyl migration, which, from analogy with the behaviour of

FIG. 1. *Derivatives of* 4 : 5-*Dimercaptopentanol.*



I : $CH_2(SH)\cdot CH(SH)\cdot [CH_2]_3\cdot OAc$.
II : $CH_2(SAc)\cdot CH(SAc)\cdot [CH_2]_3\cdot OH$.

FIG. 2. *Derivatives of* 2 : 3-*Dimercaptobutane-*1 : 4-*diol.*

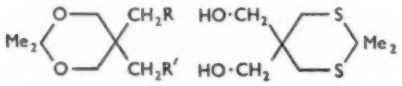


I : $CH_2(OAc)\cdot CH(SAc)\cdot CH(SAc)\cdot CH_2\cdot OAc$, m. p. 118—119°.
II : $CH_2(OAc)\cdot CH(SH)\cdot CH(SH)\cdot CH_2\cdot OAc$, m. p. 58—59°
III : $CH_2(OAc)\cdot CH(SAc)\cdot CH(SAc)\cdot CH_2\cdot OAc$, m. p. 72—73°.

4-acetylthiobutanol, was thought to be unlikely. The triacetyl compound was therefore hydrolysed to 4 : 5-dimercaptopentanol, from which the *O*-acetyl (VII) and the di-*S*-acetyl derivative (VI) were prepared by selective acetylation under acidic and basic conditions, respectively. Quantitative alkaline hydrolysis of the *O*-acetate proceeded without indication of cyclisation (see Fig. 1), thus providing conclusive evidence that it does not occur in the system under investigation; this seems to dispose of the possibility of increased nucleophilic activity of one thiol group due to the presence of a neighbouring one, but

does not, of course, prove that cyclisation in the 3 : 4-dimercaptobutanol derivatives is necessarily due to chelation. An unexpected observation, however, was the occurrence of acetyl migration on alkaline treatment of the di-*S*-acetyl derivative (VI), the liberation of thiol groups in the early stages of the hydrolysis (Fig. 1) being more rapid than the removal of acetyl groups; the additional thiol group must in some way assist the formation of the intermediate cyclic orthoacetate, which in this instance would contain a seven- or eight-membered ring.

3 : 4-Bisacetylthiopentyl acetate (VIII) would be of interest for cyclisation studies as a compound analogous to the triacetyl derivative of 3 : 4-dimercaptobutanol, but with both groups secondary. It is unlikely that the required compound could be prepared from 3 : 4-dibromopentyl acetate, because attempts to replace a vicinal pair of secondary bromine atoms by mercapto- or acetylthio-groups have usually resulted only in debromination, and formation of the corresponding olefin.[4,5] We therefore attempted to synthesise it by the addition of thiolacetic acid to pent-3-yn-1-yl acetate (IX), following the procedure which had been successful [6] with alk-1-ynes and also [7] with acetylenedicarboxylic acid. Pent-3-yn-1-ol has previously been prepared [8] in several stages from tetrahydrofuran, but the recently improved preparation [9] of propyne rendered feasible



(XVIII)

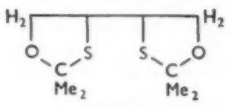
(XII; R = SAc, R′ = OAc)
(XIII; R = OTs, R′ = OTs)
(XIV; R = SAc, R′ = OTs)
(XV; R = SAc, R′ = SAc)
(XVI; R = OTs, R′ = OH)
(XVII; R = OTs, R′ = OAc)

$MeO_2C{\cdot}CH(SAc){\cdot}CH(SAc){\cdot}CO_2Me$

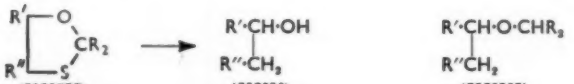
(XIX)

$CH_2(OR'){\cdot}CH(SR){\cdot}CH(SR){\cdot}CH_2{\cdot}OR'$

(XX; R = R′ = H)
(XXI; R = R′ = Ac)
(XXII; R = H; R′ = Ac)



(XXIII)



(XXIV) (XXV) (XXVI)

the direct formation of the acetylenic alcohol by interaction of propyne (made *in situ*) with ethylene oxide in liquid ammonia. Acetylation of the product gave the required acetate (IX) which was then heated for several hours at 100° with an excess of thiolacetic acid in the presence of ascaridole. The product was almost entirely a mono-adduct, for which two structures are possible depending on the direction of addition. On treatment with 2 : 4-dinitrophenylhydrazine in ethanolic sulphuric acid it gave an essentially homogeneous 2 : 4-dinitrophenylhydrazone of a hydroxypentanone. This was shown by direct comparison not to be that of 5-hydroxypentan-2-one, and must therefore be the derivative of 1-hydroxypentan-3-one (XI), derived from 3-acetylthiopent-3-en-1-yl acetate (X). Prolongation of the reaction, or re-treatment of the mono-adduct, failed to yield any appreciable amount of di-adduct. The ultraviolet light absorption of the mono-adduct (max. 2260 Å, ε 4250) is anomalous, in that it corresponds quite closely to that of a saturated monothiolacetate; all the compounds reported by Bader *et al.*,[6] containing the

[4] Rosenheim and Stadler, *Ber.*, 1905, **38**, 2687.
[5] Evans, Fraser, and Owen, *J.*, 1949, 248.
[6] Bader, Cross, Heilbron, and Jones, *J.*, 1949, 619; Bader, *J.*, 1956, 116.
[7] Owen and Sultanbawa, *J.*, 1949, 3109.
[8] Crombie and Harper, *J.*, 1950, 873.
[9] Allan, Jones, and Whiting, *J.*, 1955, 1862.

chromophore ·CH:CH·SAc, showed maxima at *ca.* 2510 Å (ε *ca.* 8000), and it is surprising that increased substitution on the ethylenic carbon atom should nullify the conjugative effect of the double bond.

Although the acetyl derivatives of 3-mercaptopropanol do not cyclise on alkaline hydrolysis, such a reaction might occur more readily in a ββ-disubstituted system, and attempts were therefore made to synthesise the derivative (XII) of thiopentaerythritol. Bladon and Owen [10] found that the ditoluene-*p*-sulphonate (XIII) of *O-iso*propylidenepentaerythritol reacted with potassium thiolacetate to give the thiolacetate toluene-*p*-sulphonate (XIV), which on prolonged further treatment gave the bisthiolacetate (XV). Two routes therefore appeared to be available: (i) replacement of the toluene-*p*-sulphonyloxy-group in the derivative (XIV) by acetoxy; and (ii) replacement of one group in the diester (XIII) by acetoxy, followed by replacement of the other by acetylthio. All attempts to introduce the acetoxy-group, however, using potassium acetate, sodium acetate, or silver acetate with the esters (XIII) or (XIV), were unsuccessful, as were experiments in which the dimethanesulphonate was used instead of the ditoluene-*p*-sulphonate; the starting materials were largely recovered. This remarkable lack of reactivity in a primary toluene-*p*-sulphonate must be attributed to the *neo*pentyl type of structure,[11] and the fact that replacement does occur (though only slowly) when the entering group is acetylthio is evidently a reflection of the much greater nucleophilic reactivity shown by the acetylthio than by the acetoxy-ion. A third route was then investigated: partial esterification of mono-*O-iso*propylidenepentaerythritol with toluene-*p*-sulphonyl chloride gave a crystalline monotoluene-*p*-sulphonate (XVI), acetylation of which furnished the acetate toluene-*p*-sulphonate (XVII); although this compound slowly reacted with potassium thiolacetate, no pure product could be isolated. The possibility of effecting replacement of a toluene-*p*-sulphonyloxy-group by solvolysis was considered, but in a trial experiment the ditoluene-*p*-sulphonate (XIII) was unchanged after 12 hours' treatment with boiling thiolacetic acid.

In the course of the above investigations, we re-examined the hydrolysis of di-*S*-acetyl-*O-iso*propylidenedithiopentaerythritol (XV) under both acid and alkaline conditions. Acid hydrolysis was accompanied by migration of the *iso*propylidene group and gave S-*iso*propylidenedithiopentaerythritol (XVIII), in agreement with the earlier work; [10] none of this material could be detected, however, in the product obtained under alkaline conditions, and it seems probable that in the original experiment, in which migration was claimed to occur, the product was allowed to become acid at some stage in the working-up process.

For reasons mentioned above, aliphatic vicinal disecondary thiols are not readily accessible, and an earlier attempt [5] to prepare the tetra-acetyl derivative of 2 : 3-dimercaptobutane-1 : 4-diol, by reaction of *meso*-1 : 4-diacetoxy-2 : 3-dibromobutane with potassium thiolacetate, gave only 1 : 4-diacetoxybut-2-ene. The required product would be readily accessible if it were possible to add two mols. of thiolacetic acid to 1 : 4-diacetoxybut-2-yne, but although some reaction occurred no pure material could be isolated. Owen and Sultanbawa,[7] however, condensed methyl acetylenedicarboxylate with an excess of thiolacetic acid and obtained two stereoisomeric forms of methyl αα′-bisacetylthiosuccinate (XIX). By reduction of each of these with lithium aluminium hydride we have now obtained the corresponding forms of 2 : 3-dimercaptobutane-1 : 4-diol (XX). The higher-melting ester gave an oil which could not be distilled without decomposition, but which furnished a crystalline tetra-acetyl derivative (XXI) whilst partial acetylation under acid conditions gave 1 : 4-diacetoxy-2 : 3-dimercaptobutane (XXII). Condensation of the oil with acetone gave a di*iso*propylidene derivative for which the most likely structure is (XXIII); on desulphurisation with Raney nickel it gave butane-1 : 4-diol, in agreement with the reports [12] that hemithioketals (XXIV) usually yield the free alcohol (XXV)

[10] Bladon and Owen, *J.*, 1950, 585.
[11] Dostrovsky, Hughes, and Ingold, *J.*, 1946, 187.

XUM

rather than the expected ether (XXVI). Reduction of the lower-melting bisacetylthiosuccinate with lithium aluminium hydride showed that this ester was not stereochemically pure, since it gave a partly crystalline product the liquid portion of which gave a tetra-acetyl and a di*iso*propylidene derivative identical with those described above; the major part was the solid stereoisomeric dihydroxy-dithiol, which gave a tetra-acetyl derivative and a di*iso*propylidene derivative. Quantitative alkaline hydrolysis of the various acetyl derivatives showed that they cyclised readily, the tetra-acetyl derivative and the di-*O*-acetate of the liquid dihydroxy-dithiol to the extent of about 50%, and the tetra-acetyl derivative of the solid isomer to the extent of about 75% (see Fig. 2).

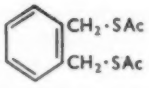
The favourable effect on cyclisation of the presence of a vicinal dithiol grouping is again evident in both the above stereoisomers, as it is in 2 : 3-dimercaptopropanol,[2] since the acetyl derivatives of 2-mercaptoethanol cyclise only to the extent of about 30%. It was thus of interest to examine the behaviour of 2-acetoxy-1 : 3-bisacetylthiopropane (XXVII) in comparison with 2 : 3-bisacetylthiopropyl acetate (XXVIII), since although the former contains no vicinal dithiol system the acetoxy-group is liable to attack from both sides. Surprisingly, quantitative alkaline hydrolysis proceeded normally, without any appreciable cyclisation. Even on treatment with boiling aqueous sodium carbonate it gave only a very small amount of 3-acetylthiopropylene sulphide (XXIX), which with this reagent is obtained [1] in good yield from the 2 : 3-isomer. The lack of reactivity is remarkable, as some cyclisation would be expected from analogy with the behaviour of 2-acetylthioethyl acetate.

The cyclisation which occurs in the hydrolysis of acetylated hydroxy-thiols involves displacement of the acetoxy-group (alkyl–oxygen fission) by a thiol anion.[2] If the oxygen functions are present as methyl ethers, instead of acetates, alkaline hydrolysis proceeds normally. Thus no difficulty was experienced [13] in the isolation of polymethoxy-dithiols by alkaline hydrolysis of their di-*S*-acetyl derivatives. These observations indicate

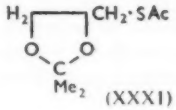
$CH_2(SAc)\cdot CH(OAc)\cdot CH_2\cdot SAc$ (XXVII)

$CH_2(SAc)\cdot CH(SAc)\cdot CH_2\cdot OAc$ (XXVIII)

$CH_2(SAc)\cdot CH\!-\!CH_2$ (XXIX)



(XXX)



(XXXI)

that there is no tendency for cyclisation to occur by displacement of an acetylthio-group (alkyl–sulphur fission) by a thiol anion, but in order to obtain more definite evidence on this point the αω-bisthiolacetates $AcS\cdot[CH_2]_n\cdot SAc$ ($n = 2$—5) and *o*-di(acetylthiomethyl)-benzene (XXX) have now been prepared from the corresponding dibromides, and subjected to quantitative alkaline hydrolysis. All of them behaved normally, the attainment of the full thiol values on completion of the hydrolysis indicating the absence of any cyclisation.

It was incidentally observed that the acetyl groups in (XV) were unusually susceptible to acid hydrolysis, free thiol being steadily produced in N-aqueous hydrochloric acid, containing 25% dioxan, at room temperature (continuous uptake of iodine, with no stable end-point); under these conditions all the other thiolacetates studied have been relatively stable. For comparison, the *iso*propylidene derivative (XXXI) of 3-acetylthiopropane-1 : 2-diol was prepared by interaction of *O*-*iso*propylideneglycerol toluene-*p*-sulphonate with potassium thiolacetate; this also showed similar acid lability.

[13] Romo, Rozenkranz, and Djerassi, *J. Amer. Chem. Soc.*, 1951, **73**, 4961; Djerassi, Gorman, and Henry, *ibid.*, 1955, **77**, 4647.
[1] Miles and Owen, *J.*, 1950, 2934.

Experimental

Reaction of 4 : 5-*Dibromopentanol with Potassium Thiolacetate.*—Crude 4 : 5-dibromopentanol [14] (31 g.), potassium thiolacetate (31 g.), and ethanol (250 c.c.) were stirred and heated under reflux for 6 hr. under nitrogen. The solution was filtered, concentrated under reduced pressure, and diluted with water. The oil which separated was isolated by extraction with ether and distilled to give (i) 4·9 g., b. p. 70—75°/0·5 mm., and (ii) 16·2 g., b. p. 150—165°/8 × 10^{-3} mm. Extensive decomposition took place during the distillation. The higher-boiling product was redistilled, but no pure 4 : 5-bisacetylthiopentanol could be obtained. The lower-boiling material was redistilled to give tetrahydrofurfuryl thiolacetate (4·6 g.), b. p. 54—59°/0·3 mm., n_D^{22} 1·494—1·497. Chapman and Owen [15] give b. p. 107°/16 mm., n_D^{20} 1·4941.

A solution of this thiolacetate (4·4 g.) in methanol (25 c.c.) containing concentrated hydrochloric acid (2·5 c.c.) was boiled under reflux for 5 hr. Water was added and the mixture was extracted with ether to give tetrahydro-2-mercaptomethylfuran (3·0 g.), b. p. 76°/50 mm., n_D^{24} 1·4882, characterised as the phenylurethane, m. p. and mixed m. p. 98—99°. Chapman and Owen [15] obtained only a small yield by acid hydrolysis, possibly owing to losses in working-up, as the thiol co-distils with methanol.

4 : 5-*Dibromopentyl Acetate.*—A solution of pent-4-en-1-ol [16] (30 g.) in acetic anhydride (48 g.) was heated on a steam-bath for 16 hr., then cooled and poured into water. The oil which separated was isolated by extraction with ether and distilled to give the acetate (32 g.), b. p. 149—154°. Paul,[17] who used a zinc chloride catalyst, gives b. p. 150—151°. Reaction in the usual way with the calculated amount of bromine in carbon tetrachloride gave 4 : 5-dibromopentyl acetate, b. p. 92—93°/0·2 mm., n_D^{18} 1·507. Paul [17] gives b. p. 156—157°/23 mm.

4 : 5-*Bisacetylthiopentyl Acetate.*—4 : 5-Dibromopentyl acetate (25 g.), potassium thiolacetate (25 g.), thiolacetic acid (0·1 c.c.), and ethanol (250 c.c.) were stirred and heated under reflux in an atmosphere of nitrogen for 10 hr. The cooled mixture was filtered, and concentrated under reduced pressure. Water was added, and the insoluble oil was isolated by extraction with chloroform and distilled to give 4 : 5-*bisacetylthiopentyl acetate* (18·6 g.), b. p. 116°/4 × 10^{-4} mm., n_D^{18} 1·5140 (Found: C, 47·3; H, 6·6; S, 23·2. $C_{11}H_{18}O_4S_2$ requires C, 47·5; H, 6·5; S, 23·0%).

4 : 5-*Dimercaptopentanol.*—4 : 5-Bisacetylthiopentyl acetate (14·5 g.) was dissolved in methanol (95 c.c.) containing concentrated hydrochloric acid (10 c.c.), and the solution was refluxed for 3 hr. under nitrogen, then set aside overnight at room temperature, and concentrated under reduced pressure. Water was added to the residue, and the mixture was extracted with ether. The ether extracts were washed with water, dried (Na_2SO_4), and concentrated to an oil, which on distillation gave 4 : 5-*dimercaptopentanol* (4·3 g.), b. p. 102—103°/0·5 mm., n_D^{19} 1·5491 (Found: C, 39·1; H, 8·0; S, 41·6; thiol-S, 40·2. $C_5H_{12}OS_2$ requires C, 39·4; H, 7·9; S, 42·1%). There was a large viscous undistilled residue.

4 : 5-*Dimercaptopentyl Acetate.*—4 : 5-Dimercaptopentanol (0·9 g.), acetic anhydride (0·65 g.), and 10% sulphuric acid in acetic acid (0·1 c.c.) were mixed at 0° and kept at 0° for 1 hr. and at room temperature for 4 days. Water (10 c.c.) was added, and the oil which separated was isolated with ether and distilled to give 4 : 5-*dimercaptopentyl acetate* (0·7 g.), b. p. 100—101°/0·1 mm., n_D^{20} 1·5109 (Found: C, 43·1; H, 7·1; S, 32·5; thiol-S, 30·5. $C_7H_{14}O_2S_2$ requires C, 43·3; H, 7·3; S, 33·0%).

4 : 5-*Bisacetylthiopentanol.*—4 : 5-Dimercaptopentanol (3·04 g.) was dissolved in water (14 c.c.) containing sodium hydroxide (1·83 g.). Acetic anhydride (4·10 g.) was added to the solution at 0°, and the mixture was stirred at 0° for 15 min. The mixture was extracted with ether, the dried (Na_2SO_4) extract was evaporated under reduced pressure, and the residue distilled to give 4 - 5-*bisacetylthiopentanol* (3·09 g.), b. p. 150—154°/0·01 mm., n_D^{20} 1·5299 (Found: C, 45·8; H, 6·7; S, 26·8; thiol-S, 0·05. $C_9H_{14}O_3S_2$ requires C, 45·7; H, 6·8; S, 27·1%). Light absorption in ethanol: max. 2320 Å, ε 7800.

Pent-3-yn-1-ol.—A solution of sodamide in liquid ammonia (*ca.* 750 c.c.), prepared in the

[14] Paul, *Compt. rend.*, 1931, **192**, 1574.
[15] Chapman and Owen, *J.*, 1950, 579.
[16] *Org. Synth.*, Coll. Vol. III, 698.
[17] Paul, *Ann. Chim.*, 1932, **18**, 303.

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usual way from sodium (75·5 g.), was stirred during the dropwise addition of 1 : 2-dichloropropane (114 g.), and for a further 3 hr. Ethylene oxide (50 g.) in dry ether (50 c.c.) was then added, and the stirring was continued overnight to assist the evaporation of ammonia. Dry ether was added to the residue followed by ammonium chloride (50 g.) and water. The ether layer was separated, and the aqueous layer was extracted several times with ether. The dried (Na_2SO_4) extracts were concentrated, and the residue was distilled to give pent-3-yn-1-ol (20 g.), b. p. 153—158°, n_D^{16} 1·4569. Crombie and Harper [8] give b. p. 154—157°, n_D^{20} 1·4554.

Pent-3-yn-1-yl Acetate.—Pent-3-yn-1-ol (10 g.), acetic anhydride (20 c.c.), and a few drops of pyridine were mixed, and the solution was heated on a steam-bath for 6 hr., then set aside overnight, and poured into water (100 c.c.). The mixture was occasionally stirred during 30 min., and the oily upper layer was then separated and washed twice with water. The combined aqueous layer and washings were extracted once with ether, and the ethereal extract was added to the oil. The ethereal solution was dried ($CaCl_2$) and distilled to give *pent-3-yn-1-yl acetate* (13·3 g.), b. p. 65—67°/15 mm., n_D^{18} 1·4391, n_D^{22} 1·4372 (Found : C, 66·25; H, 8·15%; ∃ by hydrogenation, 1·07. $C_7H_{10}O_2$ requires C, 66·6; H, 8·0%; ∃ 1·0).

Addition of Thiolacetic Acid to Pent-3-yn-1-yl Acetate.—Pent-3-yn-1-yl acetate (3·2 g.) and thiolacetic acid (6·5 g.) were mixed, 2 drops of ascaridole were added, and the mixture was heated on the steam-bath for 4 hr. Excess of thiolacetic acid and unchanged pentynyl acetate were removed under reduced pressure, and the residue was dissolved in ether. The ethereal solution was washed once with water, once with saturated aqueous sodium hydrogen carbonate solution, and twice with water; it was then dried ($CaSO_4$) and evaporated to an oil, which after two distillations gave *3-acetylthiopent-3-en-1-yl acetate* (2·4 g.), b. p. 96°/0·1 mm., n_D^{20} 1·4905 (Found : C, 53·3; H, 7·0; S, 16·2. $C_9H_{14}O_3S$ requires C, 53·4; H, 7·0; S, 15·9%). Light absorption in ethanol : max. 2260 Å, ε 4250.

Reaction of 3-Acetylthiopent-3-en-1-yl Acetate with 2 : 4-Dinitrophenylhydrazine.—A solution of the mono-adduct (1·19 g.) in ethanol (10 c.c.) was added to 2 : 4-dinitrophenylhydrazine (2 g.) in sulphuric acid (2 c.c.) and ethanol (15 c.c.), and the mixture was set aside overnight at room temperature. Hydrogen sulphide and ethyl acetate were produced, and an orange solid was precipitated; this was collected and dried. Chromatography of small portions on alumina and on bentonite–kieselguhr showed that the compound was probably homogeneous. The bulk of it was chromatographed on alumina, benzene being used as solvent and eluant, and evaporation of the eluate under reduced pressure gave a solid, m. p. 158—160°, which on recrystallisation from chloroform–ethanol gave *1-hydroxypentan-3-one 2 : 4-dinitrophenylhydrazone*, m. p. 186° (Found : C, 46·9; H, 4·8; N, 19·8. $C_{11}H_{14}O_5N_4$ requires C, 46·8; H, 5·0; N, 19·85%). 5-Hydroxypentan-2-one was prepared by Bennett and Phillips's method [18] and converted into its 2 : 4-dinitrophenylhydrazone, m. p. 150° (lit.,[19] 150°). The m. p. of a mixture with the above isomer was 140—142°.

O-iso*Propylidene*-O-*toluene*-p-*sulphonylpentaerythritol*.—To a solution of *O-iso*propylidenepentaerythritol [10] (17·6 g.) in dry pyridine (100 c.c.) at 0°, toluene-*p*-sulphonyl chloride (20·0 g.) in dry pyridine (100 c.c.) was added slowly with stirring during 5 hr. The solution was set aside at 0° overnight, and the bulk of the pyridine was then removed under reduced pressure. Chloroform was added to the residue, and the chloroform solution was washed with dilute acid, then dried ($MgSO_4$), and concentrated under reduced pressure. The semi-solid residue (30·6 g.) was dissolved in hot methanol and cooled to give O-iso*propylidene*-O-*toluene*-p-*sulphonylpentaerythritol* (16 g.), m. p. 94° (from methanol) (Found : C, 54·2; H, 6·9; S, 9·6. $C_{15}H_{22}O_6S$ requires C, 54·5; H, 6·7; S, 9·7%). The mother liquors gave a second crop of crude product (2·1 g.).

O-*Acetyl*-O-iso*propylidene*-O-*toluene*-p-*sulphonylpentaerythritol*.—The above monotoluene-*p*-sulphonate (20·5 g.) was dissolved in dry pyridine (50 c.c.), and acetic anhydride (35 c.c.) was added. The solution was heated on a steam-bath for 10 hr., then cooled and poured into a large volume of water. The precipitate was crystallised from methanol to give O-*acetyl*-O-iso*propylidene*-O-*toluene*-p-*sulphonylpentaerythritol* (16·5 g.), m. p. 69—70° (Found : C, 54·5; H, 6·5; S, 8·9. $C_{17}H_{24}O_7S$ requires C, 54·8; H, 6·5; S, 8·6%).

Attempted Replacements of Toluene-p-sulphonyloxy-groups in Derivatives of Pentaerythritol.—(i) *O-iso*Propylidenepentaerythritol ditoluene-*p*-sulphonate [10] (9·6 g.), silver acetate (3·6 g.), and acetic anhydride (100 c.c.) were boiled under reflux for 30 min. The cooled mixture was

[18] Bennett and Phillips, *J.*, 1928, 1937.
[19] Paul and Tchelitcheff, *Compt. rend.*, 1950, **230**, 1872.

filtered, then diluted with water, stirred for 1 hr., and extracted with chloroform. Concentration of the dried (Na_2SO_4) extracts gave unchanged material (8·3 g.), m. p. and mixed m. p. 152°.

(ii) The ditoluene-*p*-sulphonate (4·9 g.), fused sodium acetate (0·9 g.), and ethanol (50 c.c.) were stirred and boiled under reflux for 20 hr. Most of the ethanol was then removed under reduced pressure and the residue worked up with water and chloroform to give unchanged material (3·5 g.).

(iii) In an experiment as (ii), but with potassium acetate, refluxed for 52 hr., unchanged material (90%) was recovered. A similar result was obtained with the dimethanesulphonate (recovery, 93%).

(iv) A solution of the ditoluene-*p*-sulphonate (0·50 g.) in thiolacetic acid (1·5 c.c.) was boiled under reflux for 12 hr. Removal of the acid under reduced pressure gave a solid which was dissolved in chloroform and washed with aqueous sodium hydrogen carbonate. Removal of the solvent gave unchanged material (0·46 g.).

(v) The toluene-*p*-sulphonate [10] of *S*-acetyl-*O*-*iso*propylidenemonothiopentaerythritol (3·9 g.), fused potassium acetate (3 g.), and acetone (40 c.c.) were stirred and boiled under reflux for 30 hr. Working up as in (ii) gave unchanged material, m. p. and mixed m. p. 93°.

(vi) The toluene-*p*-sulphonate of *O*-acetyl-*O*-*iso*propylidenepentaerythritol (16·5 g.), potassium thiolacetate (8 g.), and acetone (250 c.c.) were stirred and boiled under reflux for 4 hr. The mixture was then cooled and filtered, and the salts were washed with acetone. Concentration of the filtrate and washings gave a semi-solid residue, which was dissolved in the minimum amount of hot methanol. The cooled solution deposited unchanged material (10 g.); evaporation of the mother liquors gave an oil which on distillation gave fractions (1·5 g.), b. p. 120—130° (bath)/3 × 10^{-4} mm., n_D^{20} 1·4810—1·4780, all of which contained free thiol (Found on a middle fraction: thiol-S, 4·8%).

*Alkaline Hydrolysis of Di-S-acetyl-*O*-iso*propylidenepentaerythritol*.—The compound (2·0 g.) was treated exactly as previously described.[10] Distillation of the product gave partly crystalline material (1·06 g.), which on crystallisation from methanol furnished O-iso*propylidene*-4 : 4-*bishydroxymethyl*-1 : 2-*dithiolan* (the cyclic disulphide derived from *O*-*iso*propylidenedithiopentaerythritol) (0·1 g.), m. p. 59—60° (Found: C, 46·1; H, 6·6; S, 30·8. $C_8H_{14}O_2S_2$ requires C, 46·6; H, 6·8; S, 31·1%). Light absorption in ethanol: max. 3280 Å, ε 132; min. 2800 Å, ε 25. No other crystalline product could be isolated.

1 : 4-*Diacetoxybut*-2-*yne*.—But-2-yne-1 : 4-diol (60 g.) was added to acetic anhydride (180 g.) containing a few drops of pyridine. After the initial reaction had subsided, the mixture was heated on the steam-bath for 2 hr., then cooled and poured into an excess of saturated sodium hydrogen carbonate solution. Isolation of the product with ether gave the diacetate (61 g.), b. p. 138—140°/14 mm., n_D^{20} 1·4530, which solidified; recrystallisation from methanol gave thick needles, m. p. 25—27° (Found: C, 56·5; H, 6·0. Calc. for $C_8H_{10}O_4$: C, 56·5; H, 5·9%). Johnson,[20] who does not record the method used, reported the diacetate to be a liquid, b. p. 122—123°/10 mm., n_D^{20} 1·4611.

Reaction of 1 : 4-*Diacetoxybut*-2-*yne with Thiolacetic Acid*.—The diacetate (10 g.), thiolacetic acid (15 g.), and ascaridole (0·2 c.c.) were boiled under reflux for 4 hr., and then poured into water. The dark red oil was taken up in ether and washed with aqueous sodium hydrogen carbonate. Removal of solvent and distillation of the residue (5·5 g.) gave: (i) 2·7 g., b. p. 130—135°/10 mm., n_D^{20} 1·4562, mainly unchanged diacetate; and (ii) 1·5 g., b. p. 110—155°/1 mm., n_D^{20} 1·4700—1·5031. The higher-boiling fraction (Found: S, 17·4. Calc. for $C_{10}H_{14}O_5S$: S, 13·0. Calc. for $C_{12}H_{18}O_6S_2$: S, 19·9%) showed light-absorption max. in ethanol at 2300 Å (ε 4900).

Methyl αα′-Bisacetylthiosuccinate.—Prepared by Owen and Sultanbawa's method,[7] the two forms had m. p.s 118—120° and 69—70°; the latter was not stereochemically pure (see below). Owen and Sultanbawa recorded 119·5—120·5° and 71—72°, respectively.

2 : 3-*Dimercaptobutane*-1 : 4-*diol*.—(i) Lithium aluminium hydride (37 g.) was suspended in dry ether (750 c.c.) in a Soxhlet extraction apparatus, the thimble of which contained the higher-melting methyl αα′-bisacetylthiosuccinate (50 g.). Refluxing was continued for 6 hr. after disappearance of the ester, and the cooled mixture was then cautiously treated with water to decompose the excess of hydride and poured into dilute sulphuric acid. The ether layer was removed, and the aqueous portion was extracted continuously with ether overnight.

[20] Johnson, *J.*, 1946, 1009.

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The combined ethereal solutions were dried (Na_2SO_4) and evaporated to an oil (25 g.) (Found : thiol-S, 32·9. Calc. for $C_4H_{10}O_2S_2$: thiol-S, 41·6%), which could not be distilled without decomposition.

(ii) Similar reduction of the lower-melting ester (29 g.) with lithium aluminium hydride (25 g.) in dry ether (600 c.c.) gave a product (20·7 g.), m. p. 84—87°, which on crystallisation from ether furnished 2 : 3-*dimercaptobutane*-1 : 4-*diol* (6·75 g.), m. p. 90—92° (Found : C, 31·4; H, 6·8; O, 20·85; S, 41·2; thiol-S, 41·3. $C_4H_{10}O_2S_2$ requires C, 31·1; H, 6·5; O, 20·75; S, 41·6%). Concentration of the mother liquors gave a semi-solid residue (6·4 g.), from which the oil was drained off; this oil gave derivatives identical with those (see below) of the liquid thiol obtained in (i).

Derivatives of the Liquid 2 : 3-*Dimercaptobutane*-1 : 4-*diol*.—(i) The crude thiol (0·53 g.) was heated with acetic anhydride (4·9 g.) and a trace of sulphuric acid for 12 hr. at 100°. The solution was then concentrated under reduced pressure and the residue was treated with water and ether. Evaporation of the ethereal solution gave the *tetra-acetyl* derivative (0·9 g.), which formed prisms (from methanol), m. p. 118—119° (Found : C, 44·6; H, 6·0; S, 19·2. $C_{12}H_{18}O_6S_2$ requires C, 44·7; H, 5·6; S, 19·9%).

(ii) The crude thiol (3·1 g.), acetic anhydride (3·1 g.; 2 mol., based on thiol value), and sulphuric acid (10 mg.) were mixed at 0° and then heated at 50—70° for 6 hr. Dilution with water and extraction with ether gave an oil (3·0 g.) which partly crystallised. The solid was drained on porous tile and recrystallised from methanol to give the *di*-O-*acetyl* derivative (0·7 g.), m. p. 58—59° (Found : C, 40·15; H, 6·2; S, 26·4; thiol-S, 24·9. $C_8H_{14}O_4S_2$ requires C, 40·3; H, 5·9; S, 26·9%).

(iii) The crude thiol (5·0 g.) was dissolved in acetone (50 c.c.), concentrated hydrochloric acid (0·1 c.c.) was added, and the solution was set aside for a week. The crystals (4·0 g.) were removed, and the solution was diluted with water. The precipitate (1·1 g.) and the crystals were crystallised from methanol giving the 1 : 2-3 : 4-*diisopropylidene* derivative, m. p. 103—104° (Found : C, 51·2; H, 7·7; S, 27·7. $C_{10}H_{18}O_2S_2$ requires C, 51·2; H, 7·7; S, 27·4%).

Derivatives of the Solid 2 : 3-*Dimercaptobutane*-1 : 4-*diol*.—(i) The solid thiol (2·1 g.) was heated with acetic anhydride (25 c.c.) and fused sodium acetate (1 g.) for 15 hr. at 100°. The mixture was poured into water and stirred, and the precipitate (4·4 g.) crystallised from methanol, giving the *tetra-acetyl* derivative, m. p. 72—73° (Found : C, 44·45; H, 5·4; S, 19·7%).

(ii) A solution of the solid thiol (0·29 g.) in acetone (3 c.c.), containing a trace of sulphuric acid, was set aside for 3 weeks and then diluted with aqueous sodium hydrogen carbonate. The precipitate (0·4 g.) on recrystallisation from methanol gave the 1 : 2-3 : 4-di*iso*propylidene derivative, m. p. 92—93° (Found : C, 51·5; H, 8·0; S, 27·45%).

Desulphurisation of 1 : 2-3 : 4-*Di*-OS-iso*propylidene*-2 : 3-*dimercaptobutane*-1 : 4-*diol*.—A solution of the di*iso*propylidene derivative (1·2 g.), m. p. 103—104°, from the liquid thiol, in ethanol (20 c.c.) was stirred and boiled under reflux with Raney nickel (*ca.* 10 g.) for 3 hr. The filtered solution was evaporated at 35°/25 mm., to an oil (0·6 g.), which on distillation gave butane-1 : 4-diol, b. p. 105—115°/12 mm., n_D^{21} 1·4280—1·4380, characterised as the bis-α-naphthylurethane, m. p. and mixed m. p. 195—196° (lit.,[21] 198°).

Alkaline Hydrolysis of 2-*Acetoxy*-1 : 3-*bisacetylthiopropane*.—The triacetyl compound [22] (2 g.) was added to a warm solution of sodium hydrogen carbonate (3 g.) in water (30 c.c.). The mixture was heated at 70° (bath)/120 mm., but no cyclic sulphide distilled. When it was boiled at atmospheric pressure, however, a small amount of oil steam-distilled; this was isolated by extraction with light petroleum (b. p. 40—60°) and distilled to give 3-acetylthiopropylene sulphide (0·18 g., 15%), b. p. 130—134°/58 mm., n_D^{19} 1·5507. Light absorption in ethanol : max. 2300 Å, ε 4000. Miles and Owen [1] give b. p. 120°/35 mm., n_D^{23} 1·5500, $\lambda_{max.}$ 2290 Å (ε 3500).

In a control experiment, 2 : 3-bisacetylthiopropyl acetate [5] (2 g.) gave at atmospheric pressure the cyclic sulphide (0·9 g., 75%), b. p. 160°/80 mm., n_D^{18} 1·5503.

1 : 3-*Bisacetylthiopropane*.—1 : 3-Dibromopropane (20 g.), potassium thiolacetate (25 g.), and dry ethanol (140 c.c.) were stirred and boiled under reflux for 6 hr. under nitrogen. The cooled mixture was then poured into water, and the insoluble oil, isolated by chloroform, was distilled to give the bisthiolacetate (14 g.), b. p. 97—98°/0·5 mm., n_D^{21} 1·5220. Chapman and Owen [15] give b. p. 152°/24 mm., n_D^{24} 1·5209.

[21] Bennett and Heathcoat, *J.*, 1929, 271.
[22] Johary and Owen, *J.*, 1955, 1303.

1 : 4-*Bisacetylthiobutane*.—Prepared in a similar way from 1 : 4-dibromobutane [23] (20 g.), the *compound* (11·7 g.) had b. p. 126°/1 mm., n_D^{17} 1·5189 (Found : C, 46·9; H, 7·1; S, 30·6. $C_8H_{14}O_2S_2$ requires C, 46·6; H, 6·8; S, 31·1%).

1 : 5-*Bisacetylthiopentane*.—1 : 5-Dibromopentane [24] (9·1 g.) similarly gave the *compound* (4·6 g.), b. p. 184—187°/0·5 mm., n_D^{20} 1·5141 (Found : C, 49·3; H, 7·3; S, 28·7. $C_9H_{16}O_2S_2$ requires C, 49·1; H, 7·3; S, 29·1%).

o-*Di*(*acetylthiomethyl*)*benzene*.—o-Di(bromomethyl)benzene [25] (8·8 g.) and potassium thiolacetate (8·8 g.) were dissolved separately in the minimum volumes of cold ethanol and then mixed; reaction occurred rapidly, and was completed by heating under reflux for 15 min. The product, isolated as above, on distillation afforded the *bisthiolacetate* (7·3 g.), b. p. 140°/0·08 mm., n_D^{18} 1·5885 (Found : C, 56·5; H, 5·6; S, 25·4. $C_{12}H_{14}O_2S_2$ requires C, 56·7; H, 5·55; S, 25·2%).

3-*Acetylthio*-1 : 2-O-iso*propylidenepropane*-1 : 2-*diol*.—1 : 2-*O*-*iso*Propylidene-3-*O*-toluene-*p*-sulphonylglycerol [26] (18·5 g.), potassium thiolacetate (8 g.), and acetone (200 c.c.) were stirred and heated under reflux for 14 hr. Concentration of the filtered solution, dilution with water, and extraction with ether gave the *thiolacetate* (10·2 g.), b. p. 114°/15 mm., n_D^{22} 1·4740 (Found : C, 50·25; H, 7·6; S, 16·6. $C_8H_{14}O_3S$ requires C, 50·5; H, 7·4; S, 16·9%). Light absorption in ethanol : max. 2300 Å, ε 4560. When the compound (0·21 g.) was dissolved in methanol (10 c.c.) and diluted with 2N-hydrochloric acid, titration with 0·111N-iodine gave a rapidly fading end-point; in 2½ hr. at room temperature the uptake (5·18 c.c.) corresponded to 50% hydrolysis of the thiolacetate.

Quantitative Hydrolysis of Thiolacetates by 0·1N-*Sodium Hydroxide in* 50% *Aqueous Dioxan at* 0°.—Harding and Owen's method [2] was used, with slight modification for the derivatives of 2 : 3-dimercaptobutane-1 : 4-diol, which dissolved too slowly in the cold reaction medium for the standard procedure to be followed; for these compounds a solution of the solid in warm dioxan (50 c.c.) was added to 0·1N-sodium hydroxide in 50% aqueous dioxan (250 c.c.) at 0°, titrations then being carried out as before.

The figures following each compound below are the final constant values for the number of acetyl groups liberated, and the number of free thiol groups present, respectively; the attainment of the full thiol value (Calc. : 2·0 groups) indicates the absence of cyclisation. The slightly high values for 1 : 2-bisacetylthioethane, for which the normal method was used, are due to incomplete dissolution in the early stages of the hydrolysis.

4 : 5-Bisacetylthiopentyl acetate : 2·92, 1·98. 4 : 5-Dimercaptopentyl acetate : see Fig. 1. 4 : 5-Bisacetylthiopentanol : see Fig. 1. 2-Acetoxyl : 3-bisacetylthiopropane : 2·94, 1·98. 1 : 2-Bisacetylthioethane : [27] 2·12, 2·12. 1 : 3-Bisacetylthiopropane : 2·01, 1·96. 1 : 4-Bisacetylthiobutane : 2·00, 2·00. 1 : 5-Bisacetylthiopentane : 2·01, 2·02. o-Di(acetylthiomethyl)-benzene : 2·03. 2·03. Derivatives of 2 : 3-dimercaptobutane-1 : 4-diol : see Fig. 2.

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[23] Wilson, *J.*, 1945, 48.
[24] *Org. Synth.*, Coll. Vol. III, 692.
[25] Perkin, *J.*, 1888, **53**, 5.
[26] Tipson, Clapp, and Cretcher, *J. Amer. Chem. Soc.*, 1943, **65**, 1092.
[27] Owen and Smith, *J.*, 1951, 2973.

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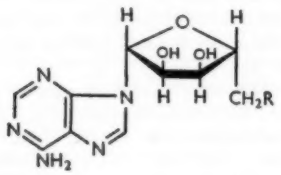
433. *Dithiols. Part XX.* The Occurrence of Transthiomethylation in Some Reactions of 2 : 3-Bismethylthiopropanol and Related Compounds.*

By Peter S. Fitt and L. N. Owen.

Treatment of 2 : 3-bismethylthiopropyl acetate with hot dilute acid gives mainly 1 : 2 : 3-trismethylthiopropane, with small amounts of 1 : 3-bismethylthiopropan-2-ol and methanethiol. The trismethylthio-compound is also formed similarly from 2 : 3-bismethylthiopropanol or its methyl ether. The probable courses of these reactions, involving sulphonium intermediates, are outlined. In the absence of a vicinal dithiol system, transthiomethylation occurs much less readily; 2-acetoxy-1 : 3-bisacetylthiopropane gives a small yield of 1 : 2 : 3-trismethylthiopropane, and 2-methylthioethanol is only slowly converted into 1 : 2-bimethylthioethane.

The importance of methylthio-compounds in certain biological processes is well recognised, and, in particular, the rôle of methionine as a methyl donor has received much attention.[1] The so-called " active methionine " (I), originally prepared [2] enzymically from methionine and adenosine triphosphate and later synthesised,[3] is of special interest because it can not only transfer a methyl group to, for example, nicotinamide, but also [4] can be hydrolysed under mild conditions to give 5′-deoxy-5′-methylthioadenosine (II); effectively, therefore, a methylthio-group has been transferred from methionine to replace a hydroxyl group in adenosine. Active methionine is very probably [4, 5] an intermediate in the microbiological formation of (II), for which an ample supply of methionine is necessary in the



I; R = $^{+}$SMe·CH$_2$·CH$_2$·CH(NH$_2$)·CO$_2^{-}$]
(II; R = SMe)

$$S\{[CH_2]_2\cdot\overset{+}{S}Me\cdot[CH_2]_2\cdot CH(NH_2)\cdot CO_2H\}_2 \xrightarrow{2H_2O} 2H^+ + S\{[CH_2]_2\cdot SMe\}_2 + 2HO\cdot[CH_2]_2\cdot CH(NH_2)\cdot CO_2H$$

(III) (IV) (V)

culture medium.[5, 6] No other instances of biological transthiomethylation appear to be known, but an earlier purely chemical example was recorded by Stein and Moore,[7] who showed that methionine reacted with 2 : 2′-dichlorodiethyl sulphide (mustard gas) in aqueous hydrochloric acid to give the sulphonium salt (III), which when heated gave 2 : 2′-di(methylthio)diethyl sulphide (IV) and 2-amino-4-hydroxybutanoic acid (V) together with much methionine; breakdown around the sulphur atom was thus occurring in two of the three possible ways. The formation of sulphonium intermediates, both by inter- and intra-molecular reactions, is of course well known in analogous systems involving groups more complex than methyl, as in mustard gas itself.[8]

* Part XIX, preceding paper.

[1] Challenger, *Quart. Rev.*, 1955, **9**, 255.
[2] Cantoni, *J. Amer. Chem. Soc.*, 1952, **74**, 2942; *J. Biol. Chem.*, 1953, **204**, 403.
[3] Baddiley and Jamieson, *J.*, 1954, 4280.
[4] Baddiley, Cantoni, and Jamieson, *J.*, 1953, 2662.
[5] Weygand, Junk, and Leber, *Z. physiol. Chem.*, 1952, **291**, 191.
[6] Smith and Schlenk, *Arch. Biochem.*, 1952, **38**, 167.
[7] Stein and Moore, *J. Org. Chem.*, 1946, **11**, 681.
[8] Stahmann, Fruton, and Bergmann, *ibid.*, p. 704; Price and Wakefield, *ibid.*, 1947, **12**, 232.

XUM

In connection with studies on the hydrolysis of acetylated hydroxy-thiols, which have revealed [9] that an *O*-acetate can undergo O–alkyl fission when displaced by a neighbouring thiol group, it was of interest to examine the behaviour of 2 : 3-bismethylthiopropyl acetate (VI). 2 : 3-Bismethylthiopropanol has been prepared [10] by selective methylation of 2 : 3-dimercaptopropanol with methyl sulphate and sodium hydroxide; we have now found that it is also formed by the use of diazomethane, the thiol groups, as expected, being preferentially methylated. Acetylation gave the acetate (VI) as a liquid; characterisation of this by oxidation with hydrogen peroxide in acetic acid resulted in simultaneous hydrolysis and gave 2 : 3-bismethylsulphonylpropanol (VII), which on reacetylation gave the disulphone corresponding to (VI). Alkaline hydrolysis of 2 : 3-bismethylthiopropyl acetate took place normally and gave 2 : 3-bismethylthiopropanol, but in boiling 0·7N-aqueous-methanolic hydrochloric acid there was a slow evolution of methanethiol (trapped and identified as its mercurichloride and mercaptide). After reaction for 3 hr. the products were isolated, but they could not be completely separated

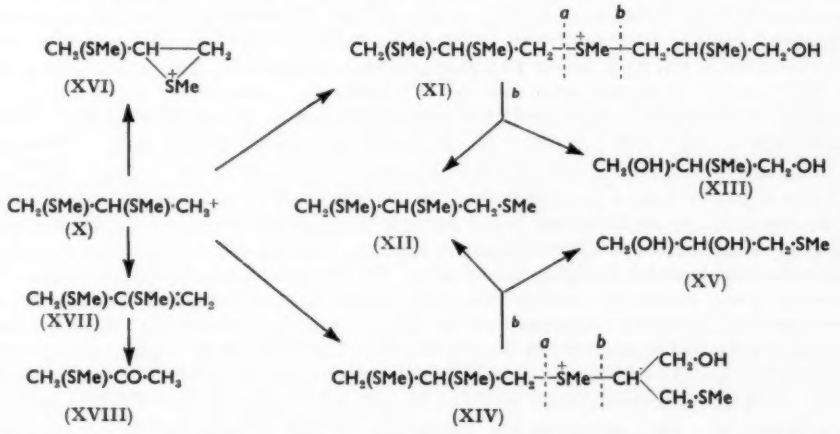
$CH_2(SMe)\cdot CH(SMe)\cdot CH_2\cdot OAc$ (VI)

$CH_2(SO_2\cdot Me)\cdot CH(SO_2\cdot Me)\cdot CH_2\cdot OH$ (VII)

$CH_2(SO_2\cdot Me)\cdot CH(SO_2\cdot Me)\cdot CH_2\cdot SO_2\cdot Me$ (VIII)

$CH_2(SO_2\cdot Me)\cdot CH(OH)\cdot CH_2\cdot SO_2\cdot Me$ (IX)

by distillation, and a puzzling feature was that the sulphur content of the higher-boiling fractions was greater than any calculated value for a likely product containing two sulphur atoms per propyl unit. The product was therefore oxidised with hydrogen peroxide in acetic acid to give a mixture of sulphones, which by a combination of extraction and fractional crystallisation was separated into three crystalline products. The major constituent was 1 : 2 : 3-trismethylsulphonylpropane (VIII), identical with authentic material prepared from propane-1 : 2 : 3-trithiol by Rheinboldt and Tetsch's method; [11] the other two were 1 : 3-bismethylsulphonylpropan-2-ol (IX), and, in smallest amount, 2 : 3-bismethylsulphonylpropanol (VII). It follows that acid hydrolysis of 2 : 3-bismethyl-



thiopropyl acetate gives mainly 1 : 2 : 3-trismethylthiopropane, with a little 1 : 3-bismethylthiopropan-2-ol, and a trace of the " normal " product. Repetition of the reaction, with 0·7N-aqueous-methanolic sulphuric acid instead of hydrochloric acid, again gave a product which on oxidation furnished the trisulphone (VIII), though in smaller yield.

[9] Fitt and Owen, preceding paper, and references there cited.
[10] Evans, Fraser, and Owen, *J.*, 1949, 248.
[11] Rheinboldt and Tetsch, *Ber.*, 1937, **70**, 680.

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From the above results it seemed likely that 2 : 3-bismethylthiopropanol itself would also undergo transthiomethylation, and when it was heated with aqueous-methanolic hydrochloric acid methanethiol was again evolved, and oxidation of the reaction product gave the trisulphone (VIII). The reaction was also carried out in the absence of organic solvent, with the same result, by heating a suspension of 2 : 3-bismethylthiopropanol in 0·7N-aqueous hydrochloric acid at 100°.

In order to determine whether etherification of the hydroxyl group would prevent the reaction, 2 : 3-bismethylthiopropyl methyl ether was synthesised by complete methylation of 2 : 3-dimercaptopropanol and also by conventional means from 2 : 3-dibromopropyl methyl ether, *via* 2 : 3-bisacetylthiopropyl methyl ether and the free dithiol. The ether proved to be much more resistant but, under the same conditions as above, methanethiol was formed, and oxidation of the product gave a small amount of the trisulphone (VIII) together with much 2 : 3-bismethylsulphonylpropyl methyl ether. Methyl ethers are not normally hydrolysed by such dilute acid, and the neighbouring sulphide group clearly has a powerful displacing effect.

The mechanism of these transthiomethylations is undoubtedly similar to those involving methionine, in that sulphonium compounds must be formed as intermediates. Under acid conditions, conversion of 2 : 3-bismethylthiopropanol, its acetate, and its methyl ether into the carbonium ion (X), followed by intermolecular attack on the sulphur atom of the primary methylthio-group of a second molecule (taken, for illustration, to be the free alcohol), would give the sulphonium ion (XI), which by breakdown at *a* or *b* respectively would either regenerate 2 : 3-bismethylthiopropanol or give the trismethylthio-compound (XII) and the monomethylthio-fragment (XIII). A similar intermolecular attack by the carbonium ion on the secondary methylthio-group would lead to the sulphonium ion (XIV), from which, according to the position of fission, either 2 : 3-bismethylthiopropanol or the trismethylthio-compound (XII) and the fragment (XV) could be formed. The sulphones derived from (XIII) and (XV) were possibly present in the liquid residues after isolation of the di- and tri-sulphones, but attempts to prove their presence were unsuccessful. The formation of 1 : 3-bismethylthiopropan-2-ol in the hydrolysis can be explained by the supposition that the carbonium ion (X) can also undergo intramolecular reaction with the neighbouring sulphur atom to give the cyclic sulphonium ion (XVI), which on fission can clearly yield either the 2 : 3- or the 1 : 3-bismethylthio-compound. The acyclic ions (XI) and (XIV) could of course arise also by a bimolecular mechanism not involving a carbonium ion, whilst the cyclic ion (XVI) could be formed by a concerted intramolecular displacement of OAc^-, OH^-, or OMe^- by the neighbouring methylthio-group. Although both uni- and bi-molecular reactions may therefore be involved, from analogy with the behaviour of mustard gas a carbonium-ion intermediate appears, however, to be favoured.

The source of the methanethiol is not immediately obvious, because its formation by breakdown of any of the possible sulphonium salts requires the simultaneous fission of the two bonds *a* and *b*, which is highly improbable. On the other hand, it appears not to be derived by direct fission of a methylthio-group from a saturated methyl sulphide, since 1 : 2-bismethylthiopropane (synthesised by direct methylation of the dithiol) was unaffected by boiling methanolic hydrochloric acid. The most likely explanation is that the carbonium ion (X) to a small extent undergoes elimination to yield the vinyl sulphide (XVII), which under acid conditions would be hydrolysed [12] to the ketone (XVIII) with loss of methanethiol. The carbonium-ion precursors of the monomethylthio-compounds (XIII) and (XV) could behave similarly. The lower-boiling fractions of the hydrolysis products did in fact give ketonic reactions, though no pure derivatives could be isolated. The number of possible products is of course not exhausted by the reactions already discussed, because other sulphonium salts, *e.g.*, derived by attack on (XIII) or (XV), can evidently be formed and lead to further by-products.

[12] Cf. Bernstein and Dorfman, *J. Amer. Chem. Soc.*, 1946, **68**, 1152; Rosenkranz, Kaufmann, and Romo, *ibid.*, 1949, **71**, 3689; Romero, Djerassi, and Rosenkranz, *ibid.*, 1951, **73**, 1528.

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The striking difference in behaviour towards alkaline hydrolysis shown by 2 : 3-bisacetylthiopropyl acetate, which readily yields an episulphide, and 2-acetoxy-1 : 3-bisacetylthiopropane, which undergoes normal hydrolysis,[9] is an illustration of the special effect which a vicinal dithiol system has upon the reactivity of a neighbouring group. It was therefore important to compare the acid hydrolysis of 2-acetoxy-1 : 3-bisacetylthiopropane (XIX) with that of the 2 : 3-isomer discussed above. Selective methylation of 1 : 3-dimercaptopropan-2-ol gave the di-*S*-methyl compound (characterised as the disulphone) which on acetylation furnished the required acetate. When this was treated as before with boiling 0·7N-aqueous-methanolic hydrochloric acid, methanethiol was again evolved; oxidation of the product gave a small proportion of the trisulphone (VIII), the material being mostly 1 : 3-bismethylsulphonylpropan-2-ol. Further evidence on this point was provided by a study of 2-methylthioethanol (XX). When this was heated with 0·7N-aqueous hydrochloric acid at 100° no methanethiol could be detected, but the formation of 1 : 2-bismethylthioethane (XXI) was evident from the characteristically obnoxious odour produced, though after 3 hr. the conversion was so small that it was not possible after oxidation to isolate the crystalline disulphone. Prolongation of the reaction for 20 hr., however, and distillation of the product, gave an oil with a sulphur content intermediate

$CH_2(SMe)\cdot CH(OAc)\cdot CH_2\cdot SMe$ (XIX)

$CH_2(SMe)\cdot CH_2R$ (XX; R = OH) (XXI; R = SMe)

$CH_2(S\cdot CH_2Ph)\cdot CH(S\cdot CH_2Ph)\cdot CH_2\cdot OH$ (XXII)

between those of (XX) and (XXI), and which on oxidation readily furnished 1 : 2-bismethylsulphonylethane. Transthiomethylation therefore occurs in these cases, but much less readily than when a vicinal bismethylthio-system is present.

In contrast to the results obtained with 2 : 3-bismethylthiopropanol, 2 : 3-bisbenzylthiopropanol (XXII) was recovered unchanged after treatment with boiling 0·7N-aqueous-methanolic hydrochloric acid. Increase in acid concentration merely resulted in the formation of 2 : 3-bisbenzylthiopropyl chloride, since oxidation of the product gave only the corresponding sulphone, no trisbenzylsulphonylpropane being detected.

Experimental

2 : 3-*Bismethylthiopropanol*.—A solution of diazomethane in *cyclo*hexane (200 c.c.), prepared from methylnitrosourea (11·4 g.), was slowly added to a stirred suspension of 2 : 3-dimercaptopropanol (2·6 g.) in *cyclo*hexane (50 c.c.). The mixture was set aside overnight, then shaken for a few minutes with acid-moistened charcoal and filtered. Concentration, and distillation of the residue, gave a main fraction (1·0 g.) of 2 : 3-bismethylthiopropanol, b. p. 89°/1 mm., n_D^{21} 1·5460. The same product was also prepared by Evans, Fraser, and Owen's method.[10] The α-naphthylurethane, recrystallised from light petroleum (b. p. 100—120°), had m. p. 84°; Evans, Fraser, and Owen gave m. p. 71°, but recrystallisation of their original specimen gave material with m. p. and mixed m. p. 82—83°.

2 : 3-*Bismethylthiopropyl Acetate*.—2 : 3-Bismethylthiopropanol (3·8 g.), fused sodium acetate (1 g.) and acetic anhydride (25 c.c.) were heated together at 100° for 8 hr. The cooled solution was then poured into water, and the oil, isolated by extraction with chloroform, on distillation afforded the *acetate* (4·9 g.), b. p. 88°/0·1 mm., n_D^{19} 1·5131 (Found: C, 43·35; H, 7·2; S, 33·3. $C_7H_{14}O_2S_2$ requires C, 43·3; H, 7·3; S, 33·0%).

2 : 3-*Bismethylsulphonylpropanol*.—(i) 2 : 3-Bismethylthiopropanol (0·6 g.) in acetic acid (2·5 c.c.) was treated dropwise with 30% hydrogen peroxide (2 c.c.). After the vigorous reaction had moderated, more hydrogen peroxide (2 c.c.) was added, and the solution was evaporated to dryness on the steam-bath. Recrystallisation of the residue from ethanol furnished the *disulphone* (0·6 g.), m. p. 123—124° (Found: C, 28·0; H, 5·7; O, 37·1; S, 29·2. $C_5H_{12}O_5S_2$ requires C, 27·8; H, 5·6; O, 37·0; S, 29·6%).

(ii) Similar treatment of 2 : 3-bismethylthiopropyl acetate (0·45 g.) gave the same product (0·5 g.), m. p. and mixed m. p. 123—124°.

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2 : 3-*Bismethylsulphonylpropyl Acetate.*—Acetyl chloride (0·4 g.) was cautiously added to a solution of the above disulphone (0·8 g.) in dry pyridine (3 c.c.). The mixture was then heated on the steam-bath for 30 min., then concentrated under reduced pressure, and diluted with water. Extraction with chloroform gave a solid (0·3 g.), which on recrystallisation from methanol afforded 2 : 3-*bismethylsulphonylpropyl acetate*, m. p. 117—119° (Found : C, 33·0; H, 5·8; O, 37·2. $C_7H_{14}O_6S_2$ requires C, 32·55; H, 5·5; O, 37·2%).

2 : 3-*Bisacetylthiopropyl Methyl Ether.*—2 : 3-Dibromopropyl methyl ether [13] (23 g.), potassium thiolacetate (25 g.), and ethanol (300 c.c.) were stirred and heated under reflux in an atmosphere of nitrogen for 2 hr. The cooled mixture was filtered, then concentrated under reduced pressure and diluted with water. The oil which separated was isolated by extraction with ether, and on distillation furnished 2 : 3-bisacetylthiopropyl methyl ether (18 g.), b. p. 72—73°/0·3 mm., n_D^{20} 1·5146. Previously prepared by another route it was reported [14] to have b. p. 158—159°/13 mm., n_D^{25} 1·5143.

2 : 3-*Dimercaptopropyl Methyl Ether.*—The above bisthiolacetate (13 g.), methanol (90 c.c.), and concentrated hydrochloric acid (10 c.c.) were boiled under reflux for 6 hr. in nitrogen. Most of the methanol was then removed under reduced pressure and the residue was diluted with water and extracted with ether to give the dithiol (4·1 g.), b. p. 57—63°/2 mm., n_D^{22} 1·515—1·518 (lit.,[15] b. p. 63—65°/6 mm., n_D^{25} 1·5178).

2 : 3-*Bismethylthiopropyl Methyl Ether.*—(i) Methyl sulphate (2·5 g.) was added dropwise to a stirred solution of the above dithiol (2·5 g.) in 30% aqueous sodium hydroxide (20 c.c.) at *ca.* 60°, under nitrogen. Stirring and heating were continued for 3 hr., and the mixture was then cooled and extracted with ether to give 2 : 3-*bismethylthiopropyl methyl ether* (1·0 g.), b. p. 110—114°/15 mm., n_D^{21} 1·5122 (Found : C, 43·7; H, 8·6; S, 37·7. $C_6H_{14}OS_2$ requires C, 43·4; H, 8·5; S, 38·6%). On oxidation with 30% hydrogen peroxide in acetic acid it gave 2 : 3-*bismethylsulphonylpropyl methyl ether*, which after recrystallisation from methanol had m. p. 112—113° (Found : C, 31·25; H, 6·3; O, 34·9. $C_6H_{14}O_5S_2$ requires C, 31·3; H, 6·1; O, 34·7%).

(ii) (With L. W. C. Miles.) Methyl sulphate (40 g.) was added, during 1 hr., to a stirred solution of 2 : 3-dimercaptopropanol (10 g.) in 30% aqueous sodium hydroxide (100 c.c.); the heat of reaction maintained the temperature at about 60°. Stirring was maintained for a further hour at 50° and for 30 min. at 100°, and the solution was then cooled and extracted with ether. Distillation of the product gave the *OSS*-trimethyl derivative (4·3 g.), b. p. 64—66°/1 mm., n_D^{20} 1·5155 (Found : S, 38·8%).

1 : 2-*Bismethylthiopropane.*—1 : 2-Dibromopropane (28 g.), potassium thiolacetate (35 g.), and ethanol (200 c.c.) were heated and stirred together under reflux for 8 hr. Concentration of the mixture, dilution of the residue with water, and extraction with ether gave 1 : 2-bisacetylthiopropane (21 g.), b. p. 79—80°/0·01 mm., n_D^{23} 1·5190. For a preparation by a different method the reported [16] constants were b. p. 93°/1 mm., n_D^{21} 1·5197.

Hydrolysis of the bisthiolacetate (19 g.) by boiling a solution in methanol (120 c.c.) and concentrated hydrochloric acid (6 c.c.) for 3 hr., followed by concentration, dilution with water, and extraction with ether, furnished 1 : 2-dimercaptopropane (3·8 g.), b. p. 52—56°/25 mm., n_D^{20} 1·527—1·531 (lit.,[17] b. p. 72—74°/55 mm.).

Methyl sulphate (7·5 g.) was slowly added to a stirred solution of this dithiol (3·8 g.) in sodium hydroxide (3 g.) and water (10 c.c.), and the temperature was finally raised to 95° for 30 min. Extraction of the cooled mixture with ether gave 1 : 2-*bismethylthiopropane* (2·1 g.), b. p. 75—76°/18 mm., n_D^{23} 1·5150 (Found : C, 44·35; H, 9·0. $C_5H_{12}S_2$ requires C, 44·1; H, 8·9%). Oxidation with 30% hydrogen peroxide in acetic acid, and recrystallisation of the product from methanol, gave 1 : 2-*bismethylsulphonylpropane*, m. p. 115—117° (Found : C, 30·1; H, 6·0; S, 31·6. $C_5H_{12}O_4S_2$ requires C, 30·0; H, 6·0; S, 32·0%).

1 : 3-*Bismethylthiopropan-2-ol.*—A stirred solution of 1 : 3-dimercaptopropan-2-ol [18] (8 g.) in 20% aqueous sodium hydroxide (40 c.c.) was treated with methyl sulphate (16 g.) during 30 min. at 75—90°. Extraction of the cooled mixture with ether gave the *di*-S-*methyl* derivative (3·5 g.), b. p. 66—68°/0·2 mm., n_D^{20} 1·5371 (Found : C, 39·4; H, 7·9; S, 41·3. $C_5H_{12}OS_2$

[13] Irvine, Macdonald, and Soutar, *J.*, 1915, **107**, 349.
[14] Bader, Cross, Heilbron, and Jones, *J.*, 1949, 619.
[15] Pavlic and Peppel, U.S.P. 2,397,689/1946.
[16] Chapman and Owen, *J.*, 1950, 579.
[17] Culvenor, Davies, and Heath, *J.*, 1949, 282.
[18] Johary and Owen, *J.*, 1955, 1303.

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requires C, 39·4; H, 7·9; S, 42·1%). Oxidation with hydrogen peroxide in acetic acid gave 1 : 3-*bismethylsulphonylpropan-2-ol*, which after recrystallisation from methanol had m. p. 133—135° (Found : C, 27·6; H, 5·7; O, 36·7. $C_5H_{12}O_6S_2$ requires C, 27·8; H, 5·6; O, 37·0%).

*2-Acetoxy-*1 : 3-*bisacetylthiopropane.*—1 : 3-Bismethylthiopropan-2-ol (3 g.), fused sodium acetate (1 g.), and acetic anhydride (20 c.c.) were heated together at 100° for 5 hr. The product, isolated as described above for the 2 : 3-isomer, on distillation gave the *acetate* (1·5 g.), b. p. 99—101°/3 mm., n_D^{20} 1·5060 (Found : C, 43·6; H, 7·2; S, 33·1. $C_7H_{14}O_2S_2$ requires C, 43·3; H, 7·3; S, 33·0%).

2-*Methylthioethanol.*[19]—Methyl sulphate (25 g.) was added to a stirred solution of 2-mercaptoethanol (15 g.) in 25% aqueous sodium hydroxide (45 c.c.) at such a rate that the temperature was maintained at 60—70°. Stirring was maintained for a further 30 min. and the product was then isolated by extraction with ether. Distillation afforded 2-methylthioethanol (11·7 g.), b. p. 61°/10 mm., n_D^{20} 1·4930 (lit.,[20] b. p. 81°/30 mm., n_D^{30} 1·4867).

Alkaline Hydrolysis of 2 : 3-*Bismethylthiopropyl Acetate.*—The acetate (1·9 g.) was vigorously stirred for 6 hr. with a solution of sodium hydroxide (4 g.) in water (50 c.c.). Extraction with ether then furnished an oil, which on distillation gave 2 : 3-bismethylthiopropanol (1·0 g.), b. p. 81°/0·02 mm., n_D^{20} 1·5462, characterised as the α-naphthylurethane, m. p. and mixed m. p. 80—82°.

Acid Hydrolysis of 2 : 3-*Bismethylthiopropyl Acetate.*—(i) The acetate (21 g.), methanol (100 c.c.), and 2N-aqueous hydrochloric acid (50 c.c.) were boiled together under reflux for 3 hr. in a slow stream of nitrogen, the gases being passed through (*a*) aqueous mercuric cyanide and (*b*) aqueous mercuric chloride. Methanethiol, m. p. 176—177° (lit., 176°), and methanethiol mercurichloride (Found : C, 4·2; H, 1·2. Calc. for $CH_3{\cdot}SHgCl$: C, 4·2; H, 1·0%) were respectively precipitated. The solution was then cooled, made alkaline with aqueous sodium hydroxide, then just acidified with hydrochloric acid and extracted continuously with ether overnight. Evaporation of the dried (Na_2SO_4) extracts gave a yellow oil (13·5 g.) which contained no free thiol and no halogen (Found : S, 43·85. Calc. for $C_5H_{12}OS_2$: S, 42·1. Calc. for $C_6H_{14}S_2$: S, 52·7%).

Repeated distillation of a portion of this oil failed to give any pure material, though a higher-boiling fraction, b. p. 139—142°/8 mm., n_D^{16} 1·5558, had a significantly high sulphur content (Found : S, 47·3%).

To a portion of the crude oil (6·7 g.), in acetic acid (60 c.c.), 30% hydrogen peroxide (60 c.c.) was added dropwise. The solution was then heated on a steam-bath for 1 hr. and evaporated to dryness. The product was stirred with 30% hydrogen peroxide (40 c.c.) and again evaporated to dryness. The crystalline residue was extracted with hot methanol, and the insoluble portion (2·86 g.), m. p. 203—205°, was recrystallised from water to give 1 : 2 : 3-trismethylsulphonylpropane, m. p. and mixed[11] m. p. 205—207° (Found : C, 26·4; H, 5·0; S, 34·5. Calc. for $C_6H_{14}O_6S_3$: C, 25·9; H, 5·1; S, 34·6%). The methanol extracts were concentrated to give a viscous residue which partly crystallised. The solid (0·9 g.) was collected, drained on a porous tile and then extracted with boiling chloroform; the insoluble residue on recrystallisation from methanol gave 1 : 3-bismethylsulphonylpropan-2-ol (0·3 g.), m. p. and mixed m. p. 132—133°. The porous tile was extracted with methanol to give a viscous brown oil (5·1 g.) which decomposed on attempted distillation.

Similar oxidation of the higher-boiling fraction mentioned above (0·4 g.) gave 1 : 2 : 3-trismethylsulphonylpropane (0·25 g.), m. p. and mixed m. p. 205—206°. Concentration of the methanolic extract and fractional crystallisation of the residue gave a few mg. of 2 : 3-bismethylsulphonylpropanol, m. p. and mixed m. p. 124—126°.

(ii) 2 : 3-Bismethylthiopropyl acetate (1 g.), methanol (10 c.c.), and 2N-aqueous sulphuric acid (5 c.c.) were boiled under reflux for 3 hr. in a slow stream of nitrogen. The product, isolated as a crude oil as described above, was oxidised in acetic acid with hydrogen peroxide to yield a mixture of sulphones (0·65 g.). This was extracted with hot methanol, and the insoluble residue (0·08 g.) on recrystallisation from water gave 1 : 2 : 3-trismethylsulphonylpropane, m. p. and mixed m. p. 207—208°. The methanol extracts were concentrated to a pasty solid, which on recrystallisation from methanol gave 2 : 3-bismethylsulphonylpropane, m. p. and mixed m. p. 124—125°. No methanethiol could be detected in the nitrogen stream.

[19] Cf. Albertson and Tullar, *J. Amer. Chem. Soc.*, 1945, **67**, 502.
[20] Kirner, *ibid.*, 1928, **50**, 2451.

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Reaction of 2 : 3-*Bismethylthiopropanol with Hydrochloric Acid.*—(i) 2 : 3-Bismethylthiopropanol (2·4 g.), methanol (10 c.c.), and 2N-aqueous hydrochloric acid (5 c.c.) were boiled together for 5 hr. in a slow stream of nitrogen. Methanethiol was evolved and detected as described above. The product on oxidation with hydrogen peroxide gave 1 : 2 : 3-trismethylsulphonylpropane (0·6 g.), m. p. and mixed m. p. 207—208°.

(ii) A suspension of 2 : 3-bismethylthiopropanol (0·8 g.) in 0·7N-aqueous hydrochloric acid (10 c.c.) was stirred at 100° for 20 hr. in a slow stream of nitrogen; methanethiol was slowly evolved. The cooled mixture was then extracted with ether to yield an oil, which on oxidation furnished the above trisulphone (0·3 g.), m. p. and mixed m. p. 205—207°.

Reaction of 2 : 3-*Bismethylthiopropyl Methyl Ether with Hydrochloric Acid.*—The ether (2·2 g.), methanol (10 c.c.), and 2N-aqueous hydrochloric acid (5 c.c.) were boiled under reflux for 5 hr. in nitrogen; methanethiol was evolved. The product on oxidation gave the same trisulphone (0·10 g.), m. p. and mixed m. p. 206—207°, and 2 : 3-bismethylsulphonylpropyl methyl ether (1·2 g.), m. p. and mixed m. p. 112—113°.

Stability of 1 : 2-*Bismethylthiopropane towards Acid Hydrolysis.*—1 : 2-Bismethylthiopropane (0·76 g.), methanol (4 c.c.), and 2N-aqueous hydrochloric acid (2 c.c.) were boiled under reflux for 3 hr. in a slow stream of nitrogen; no methanethiol could be detected. The product was oxidised to give 1 : 2-bismethylsulphonylpropane (0·76 g.), m. p. and mixed m. p. 115—117°. No other sulphone could be detected.

Reaction of 2-*Acetoxy*-1 : 3-*bisacetylthiopropane with Hydrochloric Acid.*—The acetate (0·7 g.), methanol (4 c.c.), and 2N-aqueous hydrochloric acid (2 c.c.) were boiled under reflux for 3 hr. in nitrogen; methanethiol was evolved. Oxidation of the product gave 1 : 2 : 3-trismethylsulphonylpropane (0·02 g.), m. p. and mixed m. p. 205—207°, and 1 : 3-bismethylsulphonylpropan-2-ol (0·23 g.), m. p. and mixed m. p. 134—135°.

Reaction of 2-*Methylthioethanol with Hydrochloric Acid.*—A solution of 2-methylthioethanol (2 g.) in 0·7N-aqueous hydrochloric acid (4 c.c.) was heated at 100° in nitrogen for 20 hr.; no methanethiol was detected. During the reaction an insoluble oil was gradually formed. The cooled mixture was then extracted with chloroform, and the product was distilled to give a highly odoriferous mobile liquid (0·6 g.), b. p. 63—65°/11 mm., n_D^{18} 1·5020 (Found : S, 39·2. Calc. for C_3H_8OS : S, 34·8. Calc. for $C_4H_{10}S_2$: S, 52·4%). A portion (0·25 g.) in acetic acid (1 c.c.) was oxidised with 30% hydrogen peroxide (3 c.c.), and the solid product on recrystallisation from water gave 1 : 2-bismethylsulphonylethane, m. p. and mixed m. p. 193—194° (Found : C, 26·0; H, 5·5. Calc. for $C_4H_{10}O_4S_2$: C, 25·8; H, 5·4%). Mathias [21] gives m. p. 191—192°.

Reaction of 2 : 3-*Bisbenzylthiopropanol with Hydrochloric Acid.*—(i) A solution of 2 : 3-bisbenzylthiopropanol [18] (4·5 g.) in methanol (25 c.c.) and 2N-aqueous hydrochloric acid (12·5 c.c.) was boiled under reflux for 2 hr. in nitrogen; no toluene-ω-thiol was evolved. The mixture was worked up as before to give unchanged 2 : 3-bisbenzylthiopropanol (4·3 g.) identified by oxidation to 2 : 3-bisbenzylsulphonylpropanol, m. p. and mixed m. p. 170—172°.

(ii) 2 : 3-Bisbenzylthiopropanol (4 g.), methanol (20 c.c.), and concentrated hydrochloric acid (20 c.c.) were treated as described above; no toluene-ω-thiol was evolved. The cooled mixture was diluted with water, and the oil which separated was taken up in ether. The dried (Na_2SO_4) ethereal solution was concentrated and the residue (3·5 g.) was oxidised in the usual way with 30% hydrogen peroxide. The product (1·4 g.), after recrystallisation from acetic acid, furnished 2 : 3-*bisbenzylsulphonylpropyl chloride*, m. p. 204—205° (Found : C, 52·7; H, 5·1; Cl, 9·0. $C_{17}H_{19}O_4S_2Cl$ requires C, 52·8; H, 4·95; Cl, 9·2%).

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Department of Chemistry, Imperial College of Science and Technology,
South Kensington, London, S.W.7. [*Received, December 7th*, 1956.]

[21] Mathias, *Chem. Abs.*, 1946, **40**, 2792.

434. *Volume of Mixing in Some Non-electrolyte Mixtures.*

By R. P. Rastogi and K. T. Rama Varma.

Volume of mixing has been determined for several binary mixtures of non-electrolytes. Excess volume of mixing is in qualitative agreement with Prigogine's cell-model theory. Inversion of sign occurs in the *cyclo*hexane–*cyclo*hexanol mixture which is predicted by the latest refined theory.

Prigogine's cell-model theory of solutions predicts the sign of the main excess thermodynamic functions and the relations between them by utilizing only the molecular data.[1] It does not give a quantitative picture in view of the basic assumptions involved. A more recent theory,[2] developed by Prigogine and his co-workers, combines the advantages of the cell-model theory and Longuet-Higgins's theory of conformal solutions.[3] It is an inherent advantage of the two theories that the experimentally simplest thermodynamic quantity, *viz.*, volume of mixing, can be compared against the predicted values. The object of the present paper is to test the theories for some more mixtures and get an idea about intermolecular forces in solution.

Experimental

The substances were purified by repeated distillation. Excess volume of mixing was determined from density measurements. Corrections were made for the effect of buoyancy of air and for the weight of the vapour in the pycnometer tubes. The density measurements at 30° are tabulated. Timmermans's values for pure components are given for comparison.[4b]

Mol. fract. of C_6H_6	d^{30}	Mol. fract. of C_6H_6	d^{30}	Mol. fract. of C_6H_6	d^{30}	Mol. fract. of C_6H_6	d^{30}
Benzene–toluene		*Benzene–*p*-xylene*		*Benzene–*o*-xylene*		*Benzene–*m*-xylene*	
0	0·8553	0	0·8530	0	0·8711	0	0·8560
0·2176	0·8573	0·1689	0·8544	0·2422	0·8690	0·1545	0·8565
0·3739	0·8616	0·2612	0·8552	0·3517	0·8681	0·2431	0·8570
0·5577	0·8619	0·3898	0·8567	0·4410	0·8676	0·3636	0·8577
0·7045	0·8626	0·4703	0·8575	0·6127	0·8676	0·4451	0·8587
0·8812	0·8663	0·5815	0·8590	0·7330	0·8674	0·4996	0·8593
1	0·8679	0·6517	0·8590	0·7425	0·8676	0·6160	0·8609
		0·7450	0·8621	0·8250	0·8678	0·6940	0·8622
		0·8090	0·8633	0·8868	0·8680	0·7626	0·8634
		0·8814	0·8651	0·9394	0·8682	0·8252	0·8647
		0·9282	0·8663	1	0·8679	0·9352	0·8669
		1	0·8679			1	0·8679

Mol. fract. of *p*-C_8H_{10}	d^{30}	Mol. fract. of MeOH	d^{30}	Mol. fract. of $C_6H_{12}O$	d^{30}
o-*Xylene–*p*-xylene*		*Water–methyl alcohol*		cyclo*Hexane–*cyclo*hexanol*	
0	0·8711	0·1052	0·9690	0	0·7705
0·1148	0·8689	0·1832	0·9508	0·0500	0·7780
0·1979	0·8679	0·2768	0·9271	0·1836	0·7988
0·2659	0·8663	0·3609	0·9090	0·3261	0·8238
0·3557	0·8652	0·4682	0·8919	0·3499	0·8284
0·4385	0·8629	0·4729	0·8861	0·4494	0·8472
0·5332	0·8612	0·6575	0·8450	0·5061	0·8581
0·6950	0·8583	0·7133	0·8482	0·5520	0·8652
0·8485	0·8555	0·8469	0·8189	0·6147	0·8786
0·9094	0·8547	1	0·7822	0·6609	0·8884
1	0·8530			0·8343	0·9203
				1	0·9484

Timmermans gives: benzene 0·8523; toluene 0·8577; *p*-xylene 0·8684; *o*-xylene 0·8716; *m*-xylene 0·8555; methyl alcohol 0·7818; *cyclo*hexane 0·7693.

[1] Prigogine and Mathot, *J. Chem. Phys.*, 1952, **20**, 49; Prigogine and Bellemans, *Discuss. Faraday Soc.*, 1953, **15**, 80; Mathot and Desmyter, *J. Chem. Phys.*, 1953, **21**, 782; Mathot, Staveley, Young, and Parsonage, *ibid.*, 1955, **23**, 1551.

[2] Prigogine, Bellemans, and Englert-Chowles, *J. Chem. Phys.*, 1956, **24**, 518.

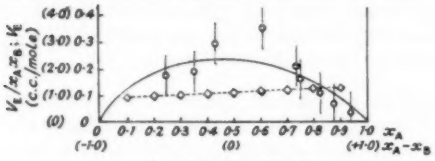
[3] Longuet-Higgins, *Proc. Roy. Soc.*, 1951, *A*, **205**, 247.

[4] (*a*) Partington, "An Advanced Treatise on Physical Chemistry," Longmans, London, 1949; (*b*) Timmermans, "Physical Constants of Pure Organic Compounds," Elsevier, Amsterdam, 1950; (*c*) Hirschfelder, Curtiss, and Bird, "Molecular Theory of Gases and Liquids," John Wiley and Sons, Inc., New York, 1954.

XUM

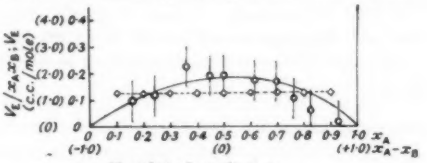
By using these values of densities, excess volumes V_E have been calculated and are plotted against mole-fractions for some cases in Figs. 1—4. The dotted curves are obtained when

FIG. 1. *Volumes of mixing in benzene–o-xylene.*



——— V_E *plotted against* x_A.
– – – – V_E/x_Ax_B *plotted against* $x_A - x_B$.

FIG. 2. *Volume of mixing in benzene–*m*-xylene.*



——— V_E *plotted against* x_A.
– – – – V_E/x_Ax_B *plotted against* $x_A - x_B$.

(Figures in parentheses refer to the scale of the latter curve.)

FIG. 3. *Volume of mixing in methyl alcohol–water.*

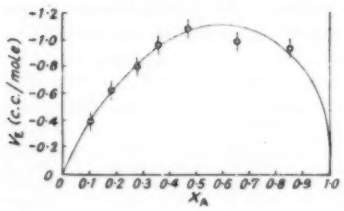
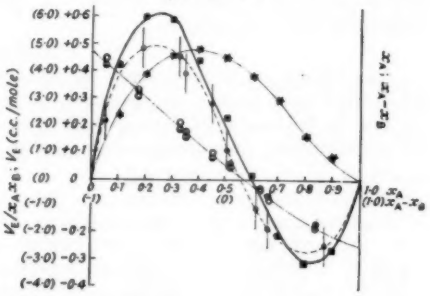


FIG. 4. *Volume of mixing in* cyclo*hexanol–* cyclo*hexane.*



○ *Experimental curve.*
✱ *Theoretical curve according to cell-model theory.*
■ *Theoretical curve according to latest refined theory.*
○ V_E/x_Ax_B, *plotted against* $x_A - x_B$ *according to proposed empirical equation.*
● V_E/x_Ax_B, *experimental.*

(Figures in parentheses refer to the plot of V_E/x_Ax_B against $x_A - x_B$.)

V_E/x_Ax_B is plotted against $(x_A - x_B)$. The following equations are found to fit the experimental curves.

For *cyclo*hexane–*cyclo*hexanol :

$$V_E = x_Ax_B[0{\cdot}42 - 3{\cdot}6(x_A - x_B) + 0{\cdot}68(x_A - x_B)^2]$$

For benzene–*o*-xylene :

$$V_E = x_Ax_B[1{\cdot}12 + 0{\cdot}2(x_A - x_B) - 0{\cdot}1(x_A - x_B)^2]$$

For benzene–*p*-xylene :

$$V_E = 0 \text{ (slightly positive)}$$

For benzene–*m*-xylene :

$$V_E = x_Ax_B[0{\cdot}76 + 0{\cdot}03(x_A - x_B) - 0{\cdot}2(x_A - x_B)^2]$$

No fit was obtained for the water–methyl alcohol system. For the rest of the systems studied, the excess volumes of mixing are negligible within experimental error.

DISCUSSION

The essential assumptions underlying the original cell-model treatment by Prigogine *et al.* (1952) are the following : (1) The molecules of the constituents A and B are spherical in shape with isotropic fields of forces. (2) The distance of maximum interaction for AA, AB, and BB pairs is about the same (this assumption has been dispensed with in subsequent papers). (3) There is random mixing. (4) The mean potential field in the cage is of the

smoothed potential type (vertical walls and flat bottom) with both depth and width depending on the concentration of the mixture. Assumption (4) has been dispensed with in the later treatment by Prigogine *et al.* (1956). In both treatments the potential is assumed to be 6–12 Lennard-Jones potential.

According to the original cell-model theory the excess volume of mixing is given by the expression :

$$\gamma V_E/(\gamma_{AA}{}^*)^3 = 0{\cdot}9161\ [4{\cdot}125\rho^2 + 0{\cdot}75\rho\delta + 1{\cdot}50\rho\delta(x_A - x_B)]x_Ax_B + 2{\cdot}032\ kT/\Lambda_{AA}[-2\theta - 0{\cdot}75\delta^2 + \theta\delta(1 + 2x_B) + \theta^2 - 10{\cdot}44\rho^2 - 3\rho\delta - 2{\cdot}55\rho\theta(x_A - x_B) + 0{\cdot}227\rho\delta]x_Ax_B] \quad . \quad . \quad . \quad . \quad . \quad (1)$$

where γ is a geometrical factor depending on the lattice assumed, $\gamma_{AA}{}^*$ is the radius of an A molecule in pure A, $\rho = (\gamma_{BB}{}^* - \gamma_{AA}{}^*)/\gamma_{AA}{}^*$ represents the difference in size of the A and B molecules, $\delta = (1/\Lambda_{AA})[\Lambda_{BB} - \Lambda]_{AA}$,

and $$\theta = (1/\Lambda_{AA})\left[\Lambda_{AB} - \frac{\Lambda_{BB} + \Lambda_{AA}}{2}\right]$$

where $\Lambda_{ij} = Z/\varepsilon_{ij}{}^*$ where Z is the number of molecules which are nearest neighbours to any given molecule, and $\varepsilon_{ij}{}^*$ represents the force constant of interaction between molecules i and j. x_A and x_B are the mole fractions of components A and B, k is Boltzmann's constant, and T is the absolute temperature.

According to the latest theory of Prigogine *et al.* the excess volume of mixing is given by the expression :

$$V_E/x_Ax_B = \tfrac{3}{2}v_{AA}\rho[\theta(x_A - x_B) + \tfrac{1}{2}\delta + \tfrac{11}{4}\rho] + Tv_{AA}'[-2\theta - 9\rho^2 + \theta^2 - \tfrac{3}{4}\delta^2 + \theta\delta(1 + 2x_B) - 3\rho\theta + \tfrac{9}{4}\rho\delta + \tfrac{3}{2}\rho\theta(x_A - x_B)] + \tfrac{1}{2}T^2v_{AA}''[\theta^2 - \tfrac{3}{4}\delta^2 + \theta\delta(1 + 2x_B)] \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (2)$$

where ρ, θ, δ, x_A, x_B, and T have the same significance as before, v_{AA} is the molar volume of the pure component A used as a reference substance, and v_{AA}' and v_{AA}'' represent first and second differentials with respect to T.

The excess volume has been calculated by using the above equations for our mixtures, except aqueous methyl alcohol. The values of the constants Λ and γ^* used in the calculation for various liquids (with *cyclo*hexane as the reference) are tabulated.

	Λ			γ^*			
Substance	from T_c	from heat of vapn.	Mean	from V_c	from d	from η	Mean
*cyclo*Hexane	1·000	1·000	1·000	1·000	1·000	1·000	1·000
Benzene	1·014	1·015	1·015	0·940	0·939	0·865	0·915
Toluene	1·0715	1·0493	1·0604	1·0075	0·994	—	1·000
o-Xylene	—	1·1467	1·1467	—	1·0375	—	1·0375
m-Xylene	—	1·1317	1·1317	—	1·044	—	1·044
p-Xylene	—	1·1247	1·1247	—	1·044	—	1·044
*cyclo*Hexanol	—	0·583	0·583	—	0·983	—	0·983

From these values, δ and ρ have been calculated and the values are again tabulated along with the calculated and experimental excess volumes for $x_A = x_B = 0{\cdot}5$.

System	δ	ρ	Excess volume * (obs.)	(calc.) eqn. (1)	(calc.) eqn. (2)	
Benzene–toluene	0·045	0·929	0	0·52	1·6	
	−0·043	−0·085		0·58	1·5	
Benzene–*m*-xylene	0·115	0·141	0·18	1·42	3·88	
Benzene–*o*-xylene	0·130	0·134	0·28	1·32	3·57	
	−0·115	−0·118		1·39	3·66	
Benzene–*p*-xylene	0·108	0·141	slightly	1·407	3·83	(30°)
	−0·098	−0·124	positive	1·502	3·70	
o-Xylene–*p*-xylene	−0·019	0·006	0	0	0	
*cyclo*Hexane–*cyclo*hexanol ...	−0·417	−0·017	—	—	—	

* The two values of excess volume for each system have been calculated by using each component as reference species respectively.

In the above calculations the values of v_{AA}, v_{AA}', and v_{AA}'' are determined from the tables given by Partington [7a] and from the values of densities at different temperatures.[7b]

The second Table indicates that for all the systems studied, the sign of the volume of mixing is predicted correctly by both the theories. Quantitative agreement is ruled out by the theories themselves in view of the restrictions imposed on the choice of the systems although the calculated excess volume by using both the equations agrees with the experimental value in the case of *o*-xylene–*p*-xylene system. Thus, benzene–*p*-xylene, etc., are not strictly spherical molecules and naturally exact quantitative agreement cannot be expected. That is probably why the values calculated by using equation (2) do not improve the agreement between theory and experiment.

Of the systems studied, *cyclo*hexane–*cyclo*hexanol mixtures conform most closely to the basic assumptions involved. *cyclo*Hexanol contains a hydroxyl group on account of which association can occur. Hence it affords a case when BB interactions are more prominent than AA or AB interactions. Obviously, this system offers a more stringent test of the theories. Accordingly we have compared the experimental volume of mixing curve with that calculated by using the two theories, in Fig. 5. In making the calculations we have used the relation, $\theta = -\delta/2$, on account of the predominance of BB interaction. It can be seen that the inversion of sign is not predicted by the cell-model theory for this system whereas the latest theory predicts it in agreement with experiment. Also the quantitative agreement is much better between theory and experiment for the latest theory.

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Lucknow University, India. [*Received, August 29th*, 1956.]

435. *The Rotatory Power of* D-(+)-*Tartaric Acid* * *and the Tartrates.*

By M. K. Hargreaves and P. J. Richardson.

The relation of the rotatory power of tartaric acid to its structure is discussed. Further measurements of the rotatory dispersion of D-tartaric acid * and its salts are reported. An attempt is made to use these results to combine the available data into a comprehensive picture.

The Solid State.—Peerdeman, van Bommel, and Bijvoet [1] showed, by an *X*-ray diffraction technique, that the conventional Fischer projection represents, fortuitously, the absolute configuration of (+)-tartaric acid. The correctness of the absolute configuration is assumed in the discussion that follows; the term "conformational isomers" refers to "rotational" isomers of the same configuration.

The relation between the rotatory power of tartaric acid in the crystalline and in the super-cooled state has recently been discussed by Levy.[2] This is of interest for the light which it might throw on the persistence of partial crystalline character in solution and the phenomena associated with "seeding" by crystals. Astbury [3] suggested that the rotatory power of tartaric acid under different conditions could be explained in terms of the persistence in solution of a spiral arrangement which he found in the crystal structure. More recent determinations by Beevers and Stern [4] do not confirm the detailed Astbury

* *I.e.*, Fischer's *d* acid.

[1] Peerdeman, van Bommel, and Bijvoet, *Proc. k. ned. Akad. Wetenschap.*, 1951, **54**, *B*, 16.
[2] Levy, *Compt. rend.*, 1949, **229**, 419.
[3] Astbury, *Proc. Roy. Soc.*, 1923, *A*, **102**, 506.
[4] Beevers and Stern, *Nature*, 1948, **162**, 854; *Acta Cryst.*, 1950, **3**, 341.

structure though their unit cell is similar. They found the space group to be $P2_1$. This implies the lack both of a centre and of planes of symmetry and the presence of a screw-diad axis. Levy [5] has argued from this that the crystal structure itself will not give rise to optical activity, and that the high rotatory power of crystalline tartaric acid is due to alignment of the individual optically active acid molecules. This argument is based on the assumption that there is no sense of screw in a screw-diad axis. This is strictly correct. But when the axis operates upon certain arrangements of points or atoms a sense of screw is produced. Fig. 1 shows that with three or more different elementary points, *e.g.*, atoms,

FIG. 1.

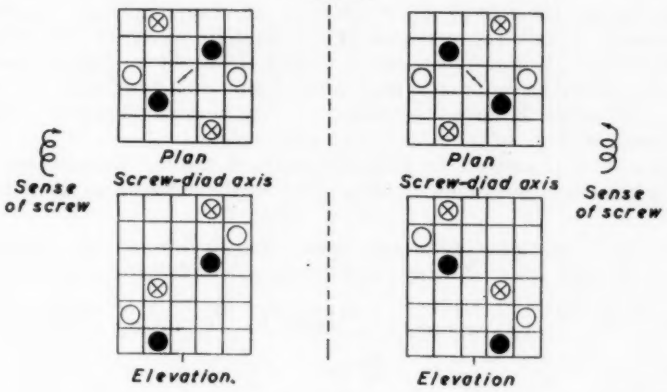
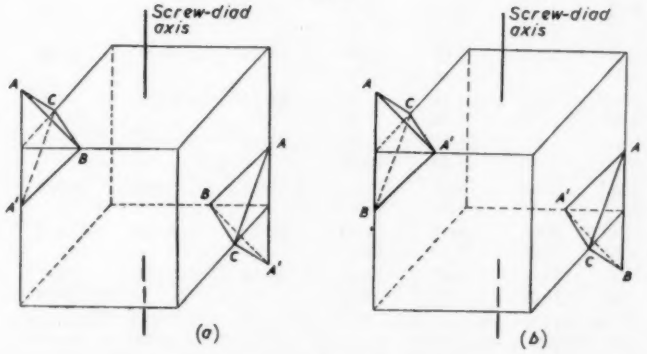


FIG. 2.



in a unit cell the presence of a screw-diad axis gives a sense of screw provided that these points do not all lie in a plane perpendicular to the screw axis and that at least two of them do not lie on a line parallel to the screw axis. When more points of the same kind are added the symmetry conditions are altered.

Fig. 2 shows the operation of a screw-diad axis on a tetrahedron in which two of the apices are the same ($A = A'$). In the first case, (*a*), there is no optical activity in the resultant structure since the two equivalent apices lie on a line parallel to the screw axis, giving rise to a plane of symmetry in the crystal. In the second case, (*b*), the structure should be optically active; Beevers and Stern's results show that the crystal of tartaric acid corresponds to this case. If A is not identical with A', the overall symmetry of the

[5] Levy, *J. Phys. Radium*, 1950, **2**, 80.

crystal of this type is not altered, so that arguments that apply to the case $A = A'$ should also apply when $A \neq A'$. Levy assumed, on the basis of the crystal structure, that the crystal of tartaric acid had no rotatory power due to the crystal framework itself; since it has been shown above that this is most unlikely, Levy's arguments would appear to be based on a misconception. A Referee has kindly pointed out that Levy's argument is disproved by the existence [6] of optically active $MgSO_4,7H_2O$ (α_{5790} 1·98°; $\alpha_D \approx 1{\cdot}8°$, per mm. orthorhombic, D_2), whose structure has only diad or screw-diad axes, and lithium sulphate monohydrate [7] (α_D 1·8° per mm., $P2_1$) which has the same space group as tartaric acid. We shall therefore not consider this theory further in this paper. Some of the criticisms of Astbury's hypothesis made by Lowry [8] and by Austin [9] are no longer valid in the light of modern theory. An adaptation of his hypothesis might therefore possibly explain the variation of the rotatory power of tartaric acid under different conditions. If the hypothesis is correct it should be possible to apply the equilibrium method to the variation of the rotatory power of tartaric acid with temperature and to obtain values for the energy difference between the crystalline form and that which is most prevalent in dilute solutions or at high temperatures.

Application of this method to Bruhat's results [10] for the super-cooled acid gives reasonable agreement in the values of ΔH and ΔS for the different wavelengths (Table 1;

TABLE 1. *Calculation of thermodynamic quantities from the variation of the rotatory power of super-cooled tartaric acid with temperature.**

Temp. (°K): $T_1 = 288{\cdot}16°$, $T_2 = 317{\cdot}16°$, $T_3 = 340{\cdot}76°$, $T_4 = 383{\cdot}03°$.
$T_1' = 288{\cdot}16°$, $T_2' = 317{\cdot}76°$, $T_3' = 332{\cdot}92°$, $T_4' = 373{\cdot}16°$.

λ (Å)	α_1, α_1'	α_2, α_2'	α_3, α_3'	α_4, α_4'	a	b	ΔH (kcal./mole)	ΔS (E.U./mole)
5840	0·71°	5·27°	8·22°	11·65°	21·83	−32·88	2282	8·8
	0·71	5·27	7·30	10·90				
5840	0·71	5·24	8·22	11·65	20·56	−24·17	2620	9·6
	0·71	5·24	7·25	10·90				
5450	−0·27	5·06	8·47	12·75	27·29	−38·65	2115	8·0
	−0·27	5·06	7·40	11·90				
5450	−0·30	5·17	8·55	12·75	24·12	−31·96	2538	9·3
	−0·30	5·17	7·50	11·90				
4680	−5·05	2·95	8·07	14·50	37·16	−66·50	1955	7·6
	−5·05	2·95	6·40	13·08				
4680	−5·05	2·95	8·07	14·50	28·43	−32·95	3228	10·9
	−5·05	2·95	6·30	13·08				
4680	−5·70	2·95	8·07	14·50	32·18	−65·84	2419	9·3
	−5·70	2·95	6·30	13·08				
4470	−7·00	1·20	6·45	14·35	61·96	−65·60	2687	8·4
	−7·00	1·20	4·80	12·80		Mean	2480	9·0

* The 6650 Å line yielded ΔH and ΔS as 3700 kcal./mole and 15·9 E.U./mole respectively. The results for this line are the least accurate since the values of α used above were interpolated from Bruhat's results by plotting α/λ and α/T. Thus the extreme points in the dispersion curve and the extreme temperatures will give less accurate results.

the method of calculation is that described earlier [11]). This is in agreement either with Levy's orientational hypothesis or with one which ascribes rotatory power to the crystal structure, provided that the absorption bands associated with the optical activity of the crystal are similar to those of the low-temperature form of the supercooled acid. The

[6] Longchambon, *Compt. rend.*, 1921, **173**, 89; Barker, "Index of Crystals," Vol. I (2), Heffer, Cambridge, 1951, O. 486.
[7] Johnsen, *Zentralblatt Mineralogie*, 1915, 233—243. Ziegler, *Z. Krist.*, 1934, **89**, 456.
[8] Lowry, "Optical Rotatory Power," Longmans, Green & Co., London, 1935, p. 292.
[9] Austin, *Trans. Faraday Soc.*, 1930, **26**, 413.
[10] Bruhat, *ibid.*, 1914, **10**, 89.
[11] Hargreaves, *J.*, 1957, 1071.

mean of the values obtained for the constant b for each wavelength follows approximately the same dispersion curve as that given by Longchambon [12] for the crystalline acid (see Table 2).

Though the rotatory constants, a and b, obtained by this method are liable to wide variation as a result of minor errors in the dispersion curve,[11] the order of magnitude obtained in this case is uniform and so probably correct. Table 1 shows that the " lower-temperature form " has a rotatory power, b, some twenty time smaller than that of the crystalline acid, and that the dispersion is similar to that of the crystalline acid. It appears, therefore, that there are at least two forms or conformations of the acid other than that of the crystal; this is in agreement with the views first expounded by Arndtsen.[13] It is notewothy that the values of ΔH lie close to those obtained by Kauzmann, Walter, and Eyring [14] for the esters of tartaric acid. Probably, therefore, at least so far as ordinary

TABLE 2.

Wavelength (Å)	5840	5450	4680	4470
$[M]$ of cryst. acid *	934°	1120°	1735°	1930°
b (molar) (=1·5b) (mean)	42·8	53·0	74·8	98·4
Ratio, $[M]/b$ (molar)	21·8	21·6	21·1	19·6

* Interpolated from Longchambon's results.[12]

temperatures are concerned, Astbury's hypothesis must be rejected. Thus in the discussion below the crystalline form has been neglected since, as it has little influence on the super-cooled acid, it may be expected to have even less on its solutions. The results are interpreted in terms of two forms or conformations associated with high and low temperatures respectively. A similar interpretation will apply to a larger number of forms provided that they fall into two groups in terms of energy.

Rotatory Power of Solutions of Tartaric Acid.—In considering the factors which may influence the rotatory power of tartaric acid first place must be given to its dissociation. Britton and Jackson [15] studied the effect of dilution and consequent ionisation on the rotatory power of solutions of tartaric acid, obtaining $[M]_D^{25} = 20{\cdot}0°$, 45·0°, and 60° for the acid, the hydrogen tartrate, and the tartrate ion respectively. They also studied the effect of adding sodium chloride to sodium tartrate solutions. They considered that the reduction in the rotatory power which they observed was due to the hydration of the sodium or chloride ions resulting in a reduction of the " free " water available for the dissolution of the tartrate. In this way the rotatory power should approximate to that observed in more concentrated solutions. Quantitatively this explanation is difficult to maintain since the change in rotatory power of 0·1M-sodium tartrate solution for a change in sodium chloride concentration from zero to 2·0M corresponds to a two-fold change in concentration [16] whilst primary solvation numbers [17] correspond to a change in concentration of 17%, and other values for the solvation numbers [18] do not alter the order of magnitude. An alternative explanation of this phenomenon is given below in the section on tartrates.

Lowry and Austin [16] have shown that the effect of increasing the concentration of a concentrated aqueous solution is to reduce the positive rotatory power in the visible region although at those concentrations the degree of ionisation is very small. Fig. 3 and Table 3 show that increase in temperature increases the positive rotatory power in the same region. Dissolution in alcohol or acetone reduces this rotatory power whilst the solutions in dioxan and ether yield negative rotations. Lowry and Austin showed that

[12] Longchambon, *Compt. rend.*, 1924, **178**, 951.
[13] Arndtsen, *Ann. Chim. Phys.*, 1858, **54**, 403.
[14] Kauzmann, Walter, and Eyring, *Chem. Rev.*, 1940, **26**, 375.
[15] Britton and Jackson, *J.*, 1934, 998.
[16] Lowry and Austin, *Phil. Trans.*, 1922, **222**, *A*, 249.
[17] Bockris and Conway, " Modern Aspects of Electrochemistry," Butterworths, London, 1954, p. 62.
[18] Robinson and Stokes, " Electrolyte Solutions," Butterworths, London, 1955, pp. 121, 320.

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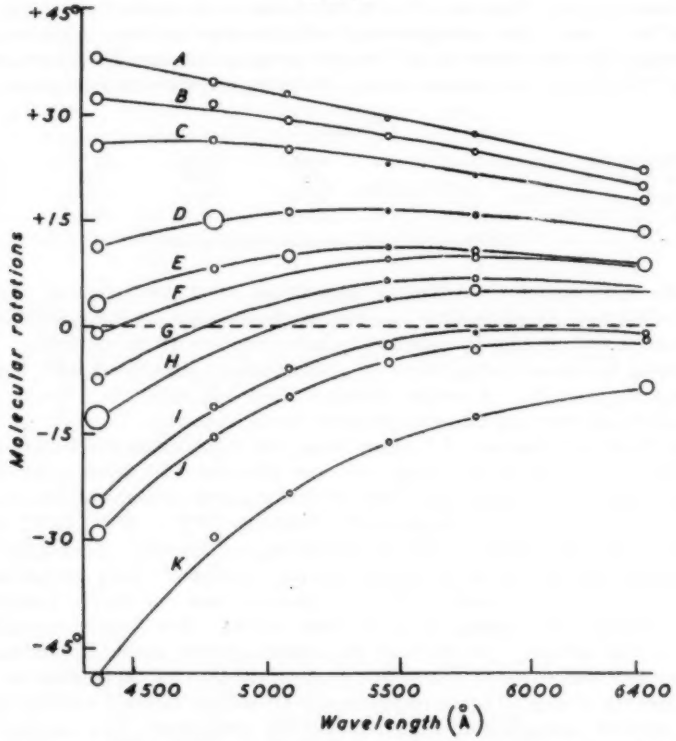
the positive rotation constant B of the Drude equation, $[\alpha] = A/(\lambda^2 - \lambda_a^2) + B/(\lambda^2 - \lambda_b^2)$, is associated with absorption in the Schumann region and that the band nearest the visible is negative is sign. The rotation constants of the two-term Drude equation are given in Table 4. Since measurements in solution are unlikely to be accurate enough for a direct derivation of the Drude equation the values in Table 4 are obtained by using the absorption wavelengths selected by Lowry and Austin as the most likely. The Table shows that,

FIG. 3.



A; 70·3°, water. *B*; 46·5°, water. *C*; 24·7°, water. *D*; 54·5°, alcohol. *E*; 37·0°, alcohol. *F*; 94·0°, dioxan. *G*; 24·0°, alcohol. *H*; 74·5°, dioxan. *I*; 57·5°, dioxan. *J*; 50·4°, dioxan. *K*; 24·0°, dioxan. The diameters of the circles represent the estimated experimental errors.

although the observed rotatory powers vary widely with solvent, concentration, and temperature, there is a systematic and sensible variation in the rotation constants of much smaller magnitude.

Table 4 shows that not only the rotatory power but also the dispersion varies with the solvent, implying that the proportions of the constituent species in solution also change. If the change in the rotatory dispersion is to be explained in terms of a small number of forms (or conformational isomers) of the acid, then intramolecular hydrogen bridges must play an important part in stabilising these conformations. For example, in dilute solution in ether or dioxan (Table 3) intermolecular bonding would give a random orientation which would not provide the basis for the observed variation of the rotatory power with temperature, since increase in temperature may be expected to result in greater freedom of rotation about all single bonds. The calculation, above, based on Bruhat's results,

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TABLE 3. *Variation of the molecular rotatory power of tartaric acid solutions with temperature.*

Solvent	Temp.	*c*	Wavelength (Å) 6438	5893	5780	5461	5086	4800	4358
Water	24·7°	10·00	+17·5°	—	+21·3°	+22·8°	+24·9°	+26·1°	+25·4°
	46·5	10·00	+19·5	—	+24·6	+26·9	+28·6	+31·0	+32·0
	70·3	10·00	+21·7	—	+27·1	+29·2	+32·7	+34·3	+37·8
Alcohol	24·0	10·00	—	—	+ 6·6	+ 6·0	—	—	− 7·2
	37·0	10·00	+ 8·8	—	+10·6	+11·0	+ 9·7	+ 8·1	+ 3·2
	54·5	10·00	+13·3	—	+15·8	+16·2	+15·9	+15·0	+11·2
Dioxan.....	24·0	10·00	− 8·7	—	−12·9	−16·5	−23·5	−29·7	−50·0
	50·4	10·00	− 1·8	—	− 3·3	− 5·1	−10·0	−15·7	−29·2
	57·0	10·00	+ 1·0	—	− 0·9	− 2·5	− 6·2	−11·4	−24·6
	74·5	10·00	—	—	+ 5·1	+ 4·0	—	—	−12·8
	94·0	10·00	—	—	+10·8	+10·3	—	—	−0·7
	24·8	5·00	−10·5	−12·3°	−13·7	−17·3	−24·2	−31·9	−52·2
	24·8	2·50	−10·5	−13·7	−14·5	−17·8	−24·8	−33·7	−54·4
Acetone	24·6	3·00	+ 4·3	+ 4·5	+ 4·3	+ 3·0	+ 2·2	− 1·6	−13·6
Ether	25·2	0·2	—	—	−14	−18	—	—	−54
Dimethylformamide	25·3	10·00	+ 1·8	+ 0·8	+ 0·3	− 1·1	− 4·4	− 8·4	−20·4
	47·7	10·00	+ 4·8	—	+ 4·0	+ 3·2	+ 0·04	− 2·7	−12·0
	68·3	10·00	+ 7·4	—	+ 7·5	+ 7·2	+ 5·4	+ 2·8	− 4·1

Densities. The expansion of the solutions necessitates a small correction for the higher temperatures, based on the ratio of the densities at that temperature and at 25°. Standard values for the pure solvent were used except for the following which were determined directly :

Soln. in dioxan (*c* 10), $d_4^{24\cdot0}$ 1·0680, $d_4^{50\cdot0}$ 1·0404, $d_4^{70\cdot0}$ 1·0197.
Soln. in H·CO·NMe_2 (*c* 10), $d_4^{20\cdot0}$ 0·9970, $d_4^{45\cdot0}$ 0·9738, $d_4^{69\cdot1}$ 0·9512.

TABLE 4. *Constants for a two-term Drude equation of tartaric acid.*

$\lambda_a^2 = 0{\cdot}030$, $\lambda_b^2 = 0{\cdot}074$.

The lettering refers to Tables 5 & 6. The values used were those for the 5461 and the 4358 Å line.

Solvent	*c*	Temp.	*A*	−*B*		*c*	Temp.	*A*	−*B*
Water	10	24·7°	19·51	11·20	Acetone–water...	G	24·8°	19·68	11·83
		46·5	20·80	11·35		H	24·8	18·88	12·06
		70·3	19·49	9·71		I	24·8	18·49	12·51
						J	24·8	17·88	12·44
Ethanol	10	24·0	19·64	15·07		K	25·2	18·50	13·67
		37·0	19·93	13·35					
		54·5	21·22	14·11	Pyridine–water	C	24·5	29·37	5·55
						D	23·0	29·54	5·62
Acetone	3	24·6	20·26	16·26		E	24·5	31·24	6·92
						F	24·5	30·40	6·26
Ether	0·2	25·2	30·61	21·64					
					Dioxan–water	A	25·3	18·50	11·80
Dioxan	10	24·0	18·90	19·50			49·2	19·67	11·68
		50·4	20·14	17·98			72·5	18·48	10·01
		74·5	21·37	16·98		B	25·3	18·27	12·50
		94·0	21·50	15·67					
	5	24·8	19·70	20·39	Aq. $CaCl_2$	L	25·3	8·43	10·90
	2·5	24·8	21·29	21·81			39·9	13·09	12·91
						M	25·2	14·90	11·95
Dimethyl-	10	25·3	19·06	16·19			42·8	15·34	10·97
formamide		47·7	18·97	15·14			54·6	15·54	10·45
		68·3	18·86	14·15					

Tartrates.

Salt	Solvent	*c*	Temp.	*A*	−*B*	Salt	Solvent	*c*	Temp.	*A*	−*B*
Li	Water	3·2	25·3°	28·40	11·80	Na	Water	10	25°	25·04	5·66
			40·0	27·48	7·21		Aq. dioxan	P	25	25·45	6·34
			56·5	27·57	7·20			Q	25	24·62	5·98
			73·3	28·27	7·67						
	Aq. LiCl	N	25·3	6·67	10·26						
			47·1	4·71	7·68						
			75	6·65	7·83						
			96·1	11·72	10·56						

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shows that the difference in the heat content of the proposed conformations is 2—3 kcal./mole, *i.e.*, less than that of one hydrogen bond (4—8 kcal.). In view of the number of possible inter- and intra-molecular hydrogen bonds this energy difference possibly corresponds rather to a difference in conformational potential energy than to a difference in the number of hydrogen bonds.

A clue as to how these bonds are distributed is given by the rotatory behaviour of the acid and its derivatives. The rotatory power of the acid varies widely with its concentration in water [16] (see also Table 3) as does that of ethyl tartrate,[19] whilst the rotatory powers of alkali tartrates, and of the acid in pyridine (Tables 5 and 6) vary much less with concentration [15] and very little with temperature. Further, the dispersion of the alkali tartrates is quite different from that of the acid, except when the latter is dissolved in a solvent such as pyridine, the rotational constant, in these cases, being markedly reduced for the shorter wavelengths (Table 4).

The similarity between the behaviour of the acid and that of the ester, and the agreement between the values of ΔH obtained for the acid (above) and the esters,[14] suggest that the factors determining their dispersion are similar, being both different from that of the salts. Thus if restriction of rotation resulting from intramolecular hydrogen bonding is the cause of the rotatory behaviour, this bonding appears to be present in the acid and the ester but not in the salt. The determining hydrogen bonding must therefore involve the hydrogen of the hydroxyl group and not necessarily that of the carboxyl group. Failure of the salts to show a similar effect may be due to hydration of the carboxylate ion. Examination of a model shows that two forms of intramolecular hydrogen bonding are possible in addition to any between α-hydroxyl and the carboxyl groups (cf. Lowry and Austin [20]). Interaction between the α-hydroxyl and the α′-carboxyl group, and the α′-hydroxyl and α-carboxyl group, gives a double link with the molecule held in an extended conformation rather similar to that of the crystal [4] (Plate 2). This presumably will be the form favoured at low temperature. Alternatively, interaction between the two carboxyl groups can give rise to one, and with some strain to two, hydrogen bonds, the molecule being held in a folded form (Plate 1).

Increasing the temperature of an aqueous solution of the acid appears to break the hydrogen bonds holding the molecule in the low-temperature conformation, there being formed, on the average, an almost equal number of alternative bonds; there will thus be an interchange of intra- and inter-molecular hydrogen bonds. The energy exchange of the process may also be attributed to the difference in energy of equal numbers of intra- and inter-molecular hydrogen bonds. Interchange would be facilitated by dilution with hydroxylic solvents, which partly explains the higher specific rotations obtained on dilution of an aqueous solution. Tartaric acid is unfortunately almost completely insoluble in most non-hydroxylic solvents, but in dioxan and in ether the acid is preferentially held in the low-temperature form. This behaviour is paralleled by that of keto–enol tautomers in which there is a greater proportion of the hydrogen-bridged enol form in hydrocarbon than in hydroxylic solvents, ether behaving as a hydrocarbon solvent.[21] Tartaric acid is insoluble in the higher ethers, so the effect of temperature on ethereal solutions cannot be studied. In dioxan increasing the temperature promotes more positive rotatory power in the visible region (Fig. 3; Table 3), *i.e.*, the effect is in the same direction as in the homogeneous acid or in hydroxylic solvents. On the other hand, whilst dilution with the latter increases the positive rotation in the visible region, dilution with dioxan makes it more negative.

Table 7 shows that the rotatory power (for 5461 and 4358 Å) of tartaric acid follows the same order as the dielectric constant of the solvent, except for pyridine, where it behaves as a salt, and for dimethylformamide. This relation between the rotatory power

[19] Patterson, *J.*, 1901, **79**, 180.
[20] Lowry and Austin, *Nature*, 1924, **114**, 431.
[21] Meyer, *Annalen*, 1911, **380**, 212.

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PLATE 1.

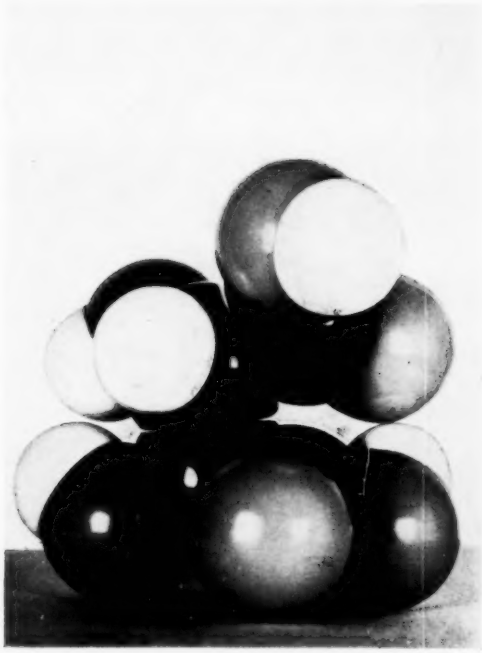
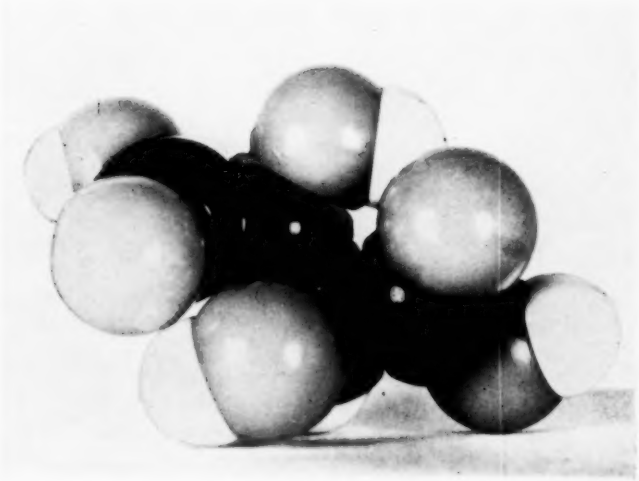


PLATE 2.



White = hydrogen, black = carbon, grey = oxygen.

[*To face p.* 2266.

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and the dielectric constant must be regarded as that between two effects with a similar cause, rather than that of cause and effect. Thus dimethylforamide, which can form only one hydrogen bond apparently has a similar isolating effect on the tartaric acid molecule as dioxan. The other hydrogen-bonding solvents, in which the rotatory power varies in the order of the dielectric constant, all have possibility of forming hydrogen-bridged chains

TABLE 5. *Molecular rotatory powers of solutions of tartaric acid* (0·66M) *in mixed solvents.*

	Solution	Concn. (M)		Temp.	Wavelength (Å) 6438	5893	5780	5461	5086	4800	4358
A	Dioxan	1·6	*a*	25·3°	+13·3°	+15·2°	+15·5°	+16·4°	+ 17·1°	+ 16·5°	+ 13·9°
	Water	42·2		49·2	+16·3	—	+19·5	+21·2	+ 22·4	+ 22·7	+ 22·2
				72·5	+18·6	—	+22·4	+24·3	+ 26·7	+ 28·2	+ 29·2
B	Dioxan	3·2	*b*	25·3	+10·5	+11·8	+12·0	+12·4	+ 12·2	+ 11·4	+ 6·5
	Water	35·9									
C	Pyridine	2·32		24·5	+59·4	—	+75·1	+84·8	+ 98·9	+111·7	+135·8
	Water	43·3									
D	Pyridine	3·41		23·0	+60·1	—	+75·8	+85·1	+ 99·2	+111·3	+136·2
	Water	38·6		44·0	+59·4	—	+74·2	+84·0	+ 98·4	+110·6	+134·2
				67·0	—	—	+73·4	+82·2	+ 94·8	+107·4	—
E	Pyridine	3·90		24·5	+59·9	—	+75·9	+85·6	+ 99·8	+112·4	+135·6
	Water	36·4									
F	Pyridine	6·10		24·5	+60·5	—	+75·7	+85·4	+100·0	+112·4	+136·0
G	Acetone	1·72		24·8	+16·0	+18·6	+19·2	+20·6	+ 22·2	+ 22·9	+ 21·0
	Water	46·00									
H	Acetone	3·57		24·8	+13·2	+15·3	+15·9	+16·6	+ 17·5	+ 16·4	+ 14·0
	Water	39·13									
I	Acetone	5·47		24·8	+10·5	+12·7	+12·9	+13·2	+ 13·1	+ 12·5	+ 7·7
	Water	32·08									
J	Acetone	6·67		24·8	+ 9·2	+10·9	+11·0	+11·2	+ 11·1	+ 9·9	+ 4·5
	Water	27·22									
K	Acetone	7·85		25·2	+ 8·4	+ 9·4	+ 9·6	+ 9·3	+ 8·2	+ 6·4	+ 0·4
	Water	22·61									

Densities. A, $d_4^{22\cdot8}$ 1·1130, $d_4^{36\cdot3}$ 1·1052, $d_4^{49\cdot4}$ 1·0974, $d_4^{63\cdot9}$ 1·0878, $d_4^{79\cdot5}$ 1·0761.
D, $d_4^{25\cdot0}$ 1·0644, $d_4^{34\cdot0}$ 1·0452, $d_4^{62\cdot0}$ 1·0397.
a, *b* Concns. of tartaric acid, (*a*) 1·3M, (*b*) 1·2M.

or aggregates, since they can form more than one hydrogen bond per molecule. The almost identical rotatory powers shown in ether (*c* 0·2) and in dioxan (*c* 2·5) are in agreement with this series since the dilution effect in ether may be expected to be similar to that in dioxan.

The dilution effect in dioxan points to the importance of intramolecular association in determining the rotatory power, since in this case the effect of rising temperature may be expected to be opposite to that of dilution, as is found (Table 3). On the other hand, dilution with a hydroxylic solvent has the same effect as rising temperature. If the determining factor were intermolecular association, however, the effect of dilution with a non-polar solvent should be similar to that of a rise in temperature. Tartaric acid is not sufficiently soluble in hydrocarbon solvents to test this, but in dioxan the effect of dilution is of opposite sign to that of rise of temperature. Since ether behaves similarly to the non-polar group in the case of keto–enol tautomerism, the behaviour of dioxan may be expected to simulate that of the non-polar group in this case (see below).

In view of the relation between the dielectric constant of hydroxylic solvents and the rotatory power of the solutions it might be expected that the effect of the addition of neutral salts to aqueous solutions of tartaric acid would follow the same law. So far as calcium chloride is concerned (Tables 6 and 7), the observed change is greater than would be expected on the basis of the depression of the dielectric constant alone, *i.e.*, by comparison with alcohol, etc. It seems probable that similar factors are involved to those

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which produce complicated behaviour in the metallic tartrates. It is noteworthy that the dispersion of the acid in calcium chloride solution and of calcium tartrate in the same medium are distinct, that of the acid resembling rather its dispersion in alcohol.

Table 5 shows that the rotatory behaviour of tartaric acid in mixed solvents is intermediate between that shown in each separately.

TABLE 6. *Molecular rotatory powers of lithium and sodium tartrate, and of tartaric acid in calcium chloride solution.*

	Soln. (aq.)	Concn. (M)	Temp.	Wavelength (Å) 6438	5893	5780	5461	5086	4800	4358
M	Acid	0·67	25·2°	—	—	+ 3·0°	+ 2·2°	—	—	− 10·0°
	$CaCl_2$	1·0	42·8	—	—	+ 8·2	+ 8·2	—	—	+ 1·2
			54·6	—	—	+11·0	+11·3	—	—	+ 7·0
L	Acid	0·67	25·3	—	—	−12·9	−17·2	—	—	− 41·3
	$CaCl_2$	1·93	39·9	—	—	− 6·7	− 8·8	—	—	− 28·5
	Li tartrate	0·20	25·3	—	—	+62·0	+69·3	—	—	+106·8
			40·0	—	—	+62·5	+70·3	—	—	+109·6
			56·5	—	—	+63·2	+70·7	—	—	+110·3
			73·3	—	—	+63·3	+71·2	—	—	+110·6
N	Li tartrate	0·05	25·3	—	—	—	−20	—	—	− 46
	LiCl	12·0	47·1	—	—	—	−17	—	—	− 37
			75	—	—	−10	−10	—	—	− 26
			96·1	—	—	− 6	− 3	—	—	− 18
	Na tartrate	0·68	25	+47·7°	+58·2°	+60·6	+68·1	+79·5°	+89·4°	+107·7
P	Na tartrate	0·68	25	+47·1	+56·7	+59·1	+66·6	+77·1	+86·7	+104·4
	Dioxan	1·45								
Q	Na tartrate	0·68	25	+46·2	+55·5	+58·5	+65·1	+75·9	+85·2	+102·3
	Dioxan	2·43								

Rotatory Power of Solutions of Metallic Tartrates.—The rotatory behaviour of the tartrates is superficially much simpler than that of the acid; this simplicity disappears, however, when the tartrates are dissolved in solutions of neutral salts, particularly those of the multivalent metals. The results quoted below are those of Darmois [22] unless given in Table 6 or otherwise stated. So far as the alkali tartrates are concerned the rotatory powers follow the same order as the molar depression of the dielectric constant of water by the alkali chlorides (Table 8). This order is the same as that of the ionic field, so that any effect which is purely electrical in origin may be expected to follow it.

Darmois has shown, however, that for the alkaline-earth tartrates the negative rotatory power increases in the order Mg < Ca < Sr < Ba, which is the reverse order to that of the alkali series. Thus, whilst the field effect no doubt influences the rotation, it is not the sole determining factor. Further, salts of the groups Zn, Cd, and Hg give rotations similar to that of sodium although their ionic fields will be quite different. In this group a mutarotation was observed, though not so marked as that of the aluminium salt. This fact, coupled with the existence of compounds of the acetylacetone-complex type [23] and with observations on the conductance of tartrates,[24] suggests that complex formation is one of the chief factors governing the rotations of these salts, and that it also influences those of the alkaline earths and possibly those of lithium and sodium. In fact, if the basis of the variation in the rotatory power of the alkali tartrates with concentration were a simple electrical-field effect, then this effect would have to be of opposite sign for the potassium, rubidium, and cæsium salts to that for the lithium and sodium salts.

If Darmois's results for the alkali tartrate series are extrapolated to zero concentration, the values $[M]^{18}_{5780}$ +62·2°, 63·0°, 64·5°, 65·7°, 64·5°, 65·1° are obtained for the Li, Na, NH_4,

[22] Darmois, *Ann. Physique*, 1928, **10**, 70.
[23] Morgan and Moss, *J.*, 1914, **105**, 195.
[24] Davies and Topp, *J.*, 1940, 87.

K, Cs, and Rb salt respectively. Each of these values should also correspond to the "molecular" rotation of the tartrate ion. Thus the alkali tartrates all give values very close to the $[M]_{5893}^{25}$ +60·0° obtained by Britton and Jackson [15] for the tartrate ion. The results for lithium tartrate (Table 6), when extrapolated to 5893 Å, give $[M]_{5893}^{25\cdot3}$ +60·3°, whilst the value $[M]_{5461}^{25\cdot3}$ +70·2° is also in agreement with the value of 70·0° given by Britton and Jackson for the tartrate ion. Thus the molecular rotatory powers of the alkali tartrates in dilute solution may be considered to be those of the tartrate ion.

TABLE 7. *Molecular rotatory powers of tartaric acid solutions and the dielectric constant* (ε) *of the solvent.*

Solvent	ε^{28}	*c*	Temp.	$[M]_{5461}$	$[M]_{4358}$	$\frac{[M]_{4358}}{[M]_{5461}}$
Water	78·5	10	24·7°	+22·8°	+ 25·4°	+ 1·11
Ethanol	24·2	10	24·0	+ 6·0	− 7·2	− 1·19
Acetone	20·4	3	24·6	+ 3·0	− 13·6	− 4·54
Ether	4·3	0·2	25·3	−18	− 54	+ 3·08
Dioxan	2·2	10	24·0	−16·5	− 50·0	+ 3·03
Aq. pyridine (D)	59·5	10	23·0	+85·1	+136·2	+ 1·60
Dimethyl formamide...	36·7	10	25·3	− 1·1	− 20·4	+18·5
Aq. $CaCl_2$ 1M	51	10	25·2	+ 3·0	− 10·0	− 3·33
1·93M	25	10	25·3	−12·9	− 41·3	+ 3·20

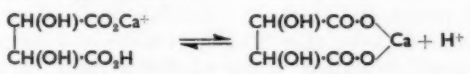
TABLE 8. *Molar depression* (δ) *of the dielectric constant* (ε) *of water by metal chlorides, and the rotatory powers of aqueous solutions of tartrates.* (δ *is determined from the equation* $\varepsilon = \varepsilon_M + 2\delta c$, *where c is the molar concentration.*)

Salt	RbCl	KCl	NaCl	LiCl	$BaCl_2$	$MgCl_2$
δ *	−5	−5	−5·5	−7	−14	−15
c	0·54	0·51	0·44	0·43	0·60	—
$[M]_{5461}^{25}$ †	67·8°	67·3°	61·8°	59·1°	34·0°	60°

* From Robinson and Stokes (ref. 18, p. 19; cf. Hasted, Ritson, and Collie, *J. Chem. Phys.*, 1948, **16**, 1). † From Darmois.[22]

If the depression due to $CaCl_2$ is similar to that of $MgCl_2$ or $BaCl_2$, the dielectric constant of 1M- and 1·93M-calcium chloride should be 51 and 25 respectively (cf. Table 7).

In considering the rotations of the alkaline-earth tartrates it is interesting that potential measurements by Cannan and Kibrick [25] appear to show the preponderance of the form on the left in the equilibrium :



Since the hydrogen-ion concentration of solutions of calcium tartrate will be low, the form on the left cannot be attained in the normal way. Also Davies and Topp [24] have shown by conductance measurements that calcium tartrate is only 75% dissociated in 0·001M-solution, whilst in the 0·025M-solutions used by Darmois the degree of dissociation is only about 4%. Davies has also attributed [26] the weak dissociation of calcium lactate to stabilisation of un-ionised complexes by co-ordination. It is clear that if the left-hand form, above, exists it has something of the hydrogen tartrate structure, but in 0·025M-solution its rotatory power is similar to that of the free tartrate ion. It is also clear from the conductivity measurements that it must exist as an ion pair with the hydroxyl group.

If this type of equilibrium exists it must involve some form of hydrolysis the degree of normal hydrolysis in these solutions being only of the order of 10^{-5}. Harned and Owen [27] have, however, used the concept of local hydrolysis to explain differences in the activites

[25] Cannan and Kibrick, *J. Amer. Chem. Soc.*, 1938, **60**, 3074.
[26] Davies, *J.*, 1938, 277.
[27] Harned and Owen, "The Physical Chemistry of Electrolytic Solutions," Reinhold Publ. Inc., New York, 1950, p. 385.
[28] Ref. 18, p. 448; Weissberger, "Organic Solvents," Interscience Publ. Inc., New York, 1955; Leader and Gormley, *J. Amer. Chem. Soc.*, 1951, **73**, 5732.

XUM

of the alkali-metal halides and their hydroxides and acetates. A similar scheme should be even more certainly applicable to the tartrates than to the acetates :

$$M^+ + OH^- \cdots H^+ \longleftarrow M^+ \cdots OH^- \cdots H^+$$

and in the presence of a proton acceptor :

$$M^+ + OH^- \cdots H^+ + A^- \longrightarrow M^+ \cdots OH^- \cdots H^+ \cdots A^-$$

where the dotted lines represent " linkages " due to ion–ion or ion–molecule forces. In the tartrates the equilibrium may take the form :

$$\begin{matrix} CH(OH)\cdot CO_2^- \\ | \\ CH(OH)\cdot CO_2^- \end{matrix} + HOH + Na^+ \rightleftharpoons \begin{matrix} CH(OH)\cdot CO_2^- \cdots H^+ \cdots OH^- \\ | \\ CH(OH)\cdot CO_2^- \cdots\cdots\cdots Na^+ \end{matrix}$$

The proximity of a proton to one carboxyl group presumably renders the other less basic, so that it remains almost completely ionised. The difference between the higher alkali-metal tartrates and those of the alkaline-earth metals appears to be that, whilst the former are completely ionised at the highest concentrations, the latter are only fully free as ions in dilute solutions and in more concentrated solutions the metal is retained by the carboxylate ion partly by co-ordination.

The increase in the rotatory powers of potassium, rubidium, and cæsium tartrate on addition of the corresponding chlorides has been attributed to hydration of the cations,[15] which reduces the " free " water available for the dissolution of the tartrate ion, thus increasing its effective concentration. This theory does not explain, however, why the molecular rotatory powers of potassium, rubidium, and cæsium tartrate increase with concentration whilst those of sodium and lithium tartrate diminish with increasing concentration. This discrepancy is particularly important since the hydration number of the lithium ion is greater than that of cæsium.[16] It seems probable that the explanation must be sought in terms of two opposing effects. Analogy with the alkaline-earth series suggests that the factor which tends to give negative rotations in the visible region is complex formation. The opposing factor may be more directly due to the ionic field. Both will increase from cæsium to lithium. In cæsium the tendency to form complexes will be very small, so that as the solution is concentrated the field effect, giving more positive rotations, may become more important. In lithium the tendency to form complexes will be greater, and is in fact dominant, so that as the concentration is increased the negative rotatory power also increases. Lithium and sodium thus represent an intermediate case. Table 6 shows that lithium tartrate in a concentrated solution of lithium chloride has a negative rotation ; if this solution is heated the rotatory power tends to become more positive. A purely electrical effect would not be expected to be so temperature-sensitive. This suggests that the presence of excess of lithium ions encourages the formation of the complex, giving rise in extreme cases to a negative rotation in the visible region ; this complex is partially disrupted by increasing the temperature.

In the alkaline-earth series the tendency to complex formation is even more marked so that in this case also the rotatory power becomes more negative as the concentration is increased.[22] The field and complex effects will both be greater with calcium than with barium, but their relative magnitudes may be different, giving rise to the reversal of the order observed in the alkali series.

It is not proposed to specify the mechanism of the " field effect." The field of a cation will influence the properties of the solution in several ways, one of which will be a direct deformation of the polarisable anion, with a resultant variation in its electron distribution and so in its rotatory power.

Conclusion.—Analysed in terms of hydrogen-bridged molecular conformations of a more or less rigid nature the behaviour of the rotatory dispersion of tartaric acid is seen to be relatively simple. The formation of complexes with the cation provides a similar explanation of the behaviour of the tartrates.

XUM

Experimental.—Observational error was less than 0·01° for 5461 and 5780 Å, and about ±0·03° for the other lines.

The tartaric acid, recrystallised from water, had m. p. 178·5—179·5°.

Solvents. These were dried as follows: acetone, $CaCl_2$; pyridine, KOH; alcohol, CaO; ether, Na; dimethylformamide, CaH_2; dioxan, refluxed over Na and freshly distilled before use.

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436. *Selective Esterification of Equatorial Hydroxyl Groups in the Synthesis of Some Methyl Ethers of* D-*Mannose.*

By G. O. ASPINALL and G. ZWEIFEL.

Methyl 4 : 6-*O*-ethylidene-α-D-mannoside (A) and 1 : 6-anhydro-β-D-mannopyranose (B). (and its 4-methyl ether), compounds for which only one chair conformation is possible, undergo selective esterification at their equatorial hydroxyl groups. By employing these reactions, 3-*O*- and 3 : 4-di-*O*-methyl-D-mannose have been synthesised and a new synthesis of 2-*O*-methyl-D-mannose has been achieved.

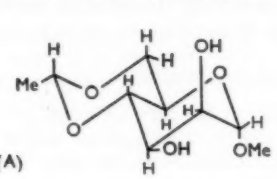
BY conventional methods, syntheses of partially methylated derivatives of D-mannose [1] have been carried out in which the hydroxyl groups in the 4 and 6, 2 and 3, and the 6 positions have been blocked. In only two cases, namely, in the syntheses of 2-*O*- [2] and 3 : 4 : 6-tri-*O*- [3] methyl-D-mannose, has it been possible to differentiate between the hydroxyl groups at $C_{(2)}$ and $C_{(3)}$. It is, however, well established that in *cyclo*hexane systems [4] equatorial secondary hydroxyl groups are more readily esterified by derivatives of carboxylic acids than are axial hydroxyl groups. We have now shown that similar preferential reactivity obtains with some sugar derivatives, of whose most stable conformations there is little doubt. Starting with methyl 4 : 6-*O*-ethylidene-α-D-mannoside (A) and 1 : 6-anhydro-β-D-mannopyranose (B) (and its 4-methyl ether), in which the D-mannopyranose rings are held in the C 1 and the 1 C conformation,[5] respectively, and by employing these selective reactions, 2- and 3-mono-*O*-, and 3 : 4-di-*O*-methyl-D-mannose have been synthesised.

Methyl 4 : 6-*O*-ethylidene-α-D-mannoside (A) [6] reacts with 1 mol. of toluene-*p*-sulphonyl chloride to give the 3-toluene-*p*-sulphonate (I) in good yield; the 2-toluene-*p*-sulphonate (VIII) could not be detected. Methylation of the 3-toluene-*p*-sulphonate (I) followed by removal of the ester group with sodium amalgam gave methyl 4 : 6-*O*-ethylidene-2-*O*-methyl-α-D-mannoside (III), hydrolysed to 2-*O*-methyl-α-D-mannose (IV). This sugar and its phenylhydrazone had similar physical constants to those reported by Pacsu and Trister.[2] The absence of a methoxyl group at $C_{(3)}$ was indicated as the derived syrupy mixture of methyl pyranosides consumed 1 mol. of periodate; the presence of methoxyl groups in positions other than 2 and 3 was precluded by the mode of synthesis.

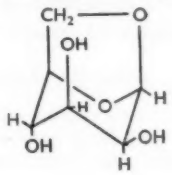
[1] For a review see Aspinall, *Adv. Carbohydrate Chem.*, 1953, **8**, 217.
[2] Pacsu and Trister, *J. Amer. Chem. Soc.*, 1941, **63**, 925.
[3] Bott, Haworth, and Hirst, *J.*, 1930, 1395.
[4] Barton, *J.*, 1953, 1027; Barton and Cookson, *Quart. Rev.*, 1956, **10**, 44.
[5] Reeves, *J. Amer. Chem. Soc.*, 1949, **71**, 215.
[6] Honeyman and Morgan, *J.*, 1954, 744.

It is of interest to compare the selective tosylation of methyl 4 : 6-*O*-ethylidene-α-D-mannoside (A) with that of methyl 4 : 6-*O*-benzylidene-α-D-glucoside.[7] The latter compound, in which the hydroxyl groups at $C_{(2)}$ and $C_{(3)}$ are both equatorial, reacts preferentially with toluene-*p*-sulphonyl chloride at position 2. Whatever explanation, steric or electronic, may be advanced for this selective reactivity, it is clear that the preferential reactivity of the equatorial 3-hydroxyl group in the D-mannose derivative can be explained on stereochemical grounds.

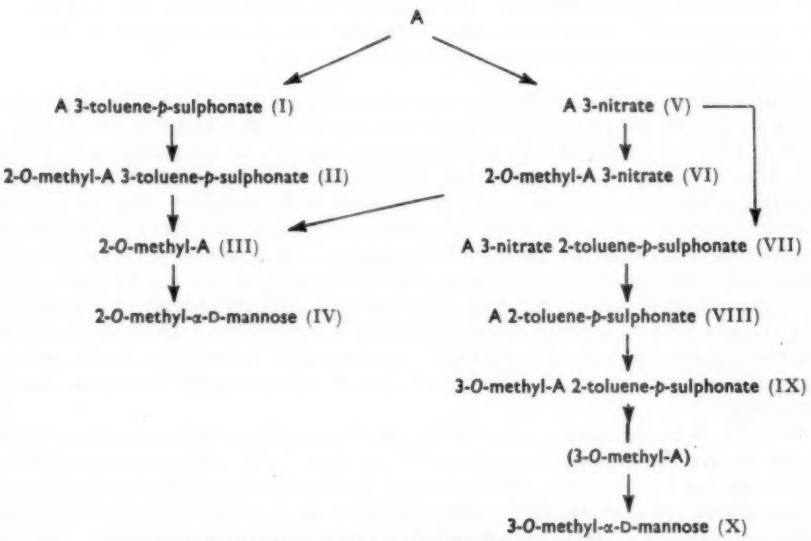
In the synthesis of 3-*O*-methyl-D-mannose (X), nitrate ester formation was used for the selective blocking of the 3-hydroxyl group. Selective esterification was not so marked in this case as it was necessary to use a large excess of nitrating reagent, but it was possible to modify the conditions used by Honeyman and Morgan [6] in the preparation of methyl 4 : 6-*O*-ethylidene-α-D-mannoside 2 : 3-dinitrate so that a reasonable quantity of the 3-nitrate (V) could be isolated; no 2-nitrate was detected. The structure of the 3-nitrate was proved by methylation followed by reductive removal of the nitrate ester to give methyl 4 : 6-*O*-ethylidene-2-*O*-methyl-α-D-mannoside (III). Tosylation of the 3-nitrate



(A)



(B)



("A" denotes methyl 4 : 6-*O*-ethylidene-α-D-mannoside)

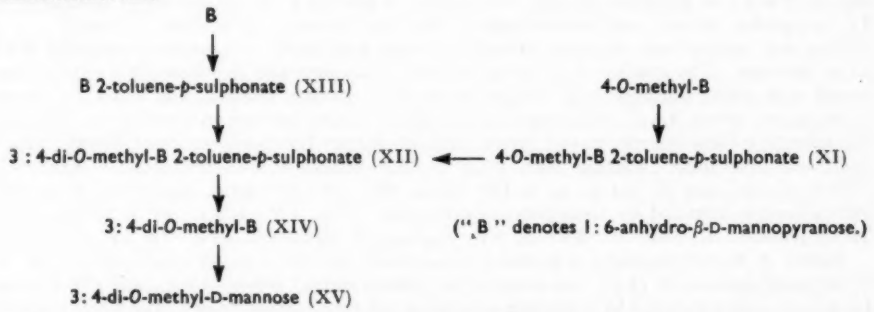
(V) followed by reductive denitration and methylation gave methyl 4 : 6-*O*-ethylidene-3-*O*-methyl-α-D-mannoside 2-toluene-*p*-sulphonate (IX). The axial toluene-*p*-sulphonate grouping in this compound was very resistant to reductive cleavage with lithium aluminium hydride (reaction was incomplete after 20 hr. in refluxing tetrahydrofuran), but the grouping was removed smoothly with sodium amalgam. Bollinger and Ulrich [8] have reported similar difficulties in the removal of the toluene-*p*-sulphonate group from

[7] Robertson and Griffith, *J.*, 1935, 1193; Bollinger and Prins, *Helv. Chim. Acta*, 1945, **28**, 465.
[8] Bollinger and Ulrich, *Helv. Chim. Acta*, 1952, **35**, 93.

methyl 4 : 6-*O*-benzylidene-3-*O*-methyl-α-D-altroside 2-toluene-*p*-sulphonate with lithium aluminium hydride; here also the ester grouping is axial. Hydrolysis of the syrupy product afforded crystalline 3-*O*-methyl-α-D-mannose (X). The structure of the sugar was confirmed by its conversion into 3-*O*-methyl-D-glucosazone and by the fact that the derived syrupy mixture of methyl pyranosides did not react with periodate.

Honeyman and Stening [9] have also prepared the 3-toluene-*p*-sulphonate (I) and the 3-nitrate (V) (but by different methods), and the 3-nitrate 2-methyl ether (VI) and the 3-nitrate 2-toluene-*p*-sulphonate (VII) of methyl 4 : 6-*O*-ethylidene-α-D-mannoside (A). We are grateful to Dr. J. Honeyman for communicating to us the results of his investigations before publication and for supplying samples of these compounds for comparison.

The synthesis of 3 : 4-di-*O*-methyl-D-mannose depended on the preferential reactivity of the 2-hydroxyl group in 1 : 6-anhydro-β-D-mannopyranose (B) and in its 4-methyl ether. Reeves [10] has shown by complex formation with cuprammonium that despite considerable non-bonded interactions (the axial 3-hydroxyl group lies in 1 : 3-relationship with the 1 : 6-anhydro-ring) both these compounds exist in the chair (1 C) rather than in the boat (3 B) conformation. Our observations agree with this result as both the anhydro-sugar (B) and its 4-methyl ether react with 1 mol. of toluene-*p*-sulphonyl chloride to give the equatorial 2-toluene-*p*-sulphonate (XIII and XI, respectively) in good yield. Both compounds (XIII and XI) yielded 1 : 6-anhydro-3 : 4-di-*O*-methyl-β-D-mannopyranose (XII) on complete methylation. It is noteworthy that under certain conditions the 4-methyl ether (XI) may be isolated during methylation of 1 : 6-anhydro-β-D-mannopyranose 2-toluene-*p*-sulphonate (XIII). An examination of models shows clearly that the 3-hydroxyl group is considerably more hindered than the axial 4-hydroxyl group which lies below the plane of the ring, and is in 1 : 3-relationship only with the axial hydrogen atom. It would be expected, therefore, that the 4- would be more reactive than the 3-hydroxyl group. Treatment of 1 : 6-anhydro-3 : 4-di-*O*-methyl-β-D-mannopyranose 2-toluene-*p*-sulphonate with sodium amalgam readily gave 1 : 6-anhydro-3 : 4-di-*O*-methyl-β-D-mannopyranose (XIV), hydrolysis of which afforded 3 : 4-di-*O*-methyl-D-mannose (XV). The sugar, isolated as the monohydrate, was identical with a sample previously isolated [11] and on oxidation yielded the known 3 : 4-di-*O*-methyl-D-mannonolactone.



These experiments show clearly that marked differences exist between the reactivities of equatorial and axial hydroxyl groups in methyl 4 : 6-*O*-ethylidene-α-D-mannoside (A) and 1 : 6-anhydro-4-*O*-methyl-β-D-mannopyranose so that the equatorial hydroxyl groups may be selectively esterfied. A similar result was found with 1 : 6-anhydro-β-D-mannopyranose (B), although in this case analogy with certain disubstituted *cyclo*hexane derivatives [12] would suggest that the equatorial 2-hydroxyl flanked by axial substituents should

[9] Honeyman and Stening, following paper.
[10] Reeves, *J. Amer. Chem. Soc.*, 1949, **71**, 2116.
[11] Aspinall, Hirst, and Warburton, *J.*, 1955, 651.
[12] Barton, *Chem. and Ind.*, 1953, 664.

be subject to greater steric compression and be less reactive than the 4-hydroxyl group. Without further knowledge of the chemistry of related compounds it is not yet possible to ascribe this result to electronic or steric factors. As far as we are aware the only example previously reported of this type of selective esterification in the carbohydrate group is the tosylation of the equatorial 3-hydroxyl group in 1 : 6-anhydro-2-*O*-benzoyl-β-D-altropyranose.[13] In this case, as with our examples, only one chair conformation is possible. It is probable that starting from stereochemically suitable compounds many partially substituted sugars, not readily accessible by other methods, may be synthesised by employing such preferential reactivity for the selective blocking of specific hydroxyl groups.

Experimental

Unless otherwise stated, chloroform solutions were dried (Na_2SO_4), evaporations were carried out under reduced pressure, and the light petroleum used had b. p. 60—80°. Chromatographic separations were carried out with columns of (*a*) activated alumina, Type H, 100/200 S mesh, supplied by Peter Spence and Sons, Ltd., and (*b*) as in (*a*) shaken with N-acetic acid, washed with water by decantation until free from acid, filtered, and dried at 260—280°. Paper partition chromatography was effected on Whatman No. 1 filter paper with (*a*) butan-1-ol–ethanol–water (4 : 1 : 5 v/v, upper layer) and (*b*) ethyl acetate–acetic acid–formic acid–water (18 : 3 : 1 : 4) as solvents.

Methyl 4 : 6-O-*Ethylidene*-α-D-*mannoside*.—Methyl α-D-mannoside (10 g.), paraldehyde (50 ml.), and concentrated sulphuric acid (0·08 ml.) were shaken at room temperature for 10 min. The solution was decanted into light petroleum (200 ml.)–saturated aqueous sodium carbonate (150 ml.). The residual methyl α-D-mannoside was treated four times with paraldehyde (25 ml.)–concentrated sulphuric acid (0·04 ml.) for periods of 10 min., and in each case the solution was decanted into the original light petroleum–sodium carbonate solution. Separation of the aqueous layer, after washing it with light petroleum (3 × 100 ml.), and evaporation yielded a white solid. Extraction of the solid with acetone and evaporation gave a syrup which crystallised from light petroleum–carbon tetrachloride (10 : 1). After three recrystallisations the mannoside (3·5 g.) had m. p. 112°, $[\alpha]_D^{17}$ +71° (*c*, 1·3 in $CHCl_3$). Honeyman and Morgan [6] give m. p. 117°, [α] +77° ($CHCl_3$).

Methyl 4 : 6-O-*Ethylidene*-α-D-*mannoside* 3-*Toluene*-p-*sulphonate* (I).—Toluene-*p*-sulphonyl chloride (2·6 g.) in pyridine (20 ml.) was added to methyl 4 : 6-*O*-ethylidene-α-D-mannoside (3 g.) in pyridine (20 ml.), and the solution was kept for 2 days at −5° and for 1 day at 0°. The solution was poured into aqueous sodium hydrogen carbonate; evaporation removed most of the pyridine. The mixture was extracted with chloroform and the chloroform extract was washed with dilute sulphuric acid, sodium hydrogen carbonate solution, and water. Concentration gave a syrup (4·5 g.) which was chromatographed from benzene on alumina (*a*). Elution with light petroleum–benzene gave a syrup (probably mainly the di-toluene-*p*-sulphonate) which would not crystallise. Elution with ether yielded *methyl* 4 : 6-O-*ethylidene*-α-D-*mannoside* 3-*toluene*-p-*sulphonate* (I) (3·1 g.), m. p. 129° (from ether–light petroleum) and mixed m. p. 125° (with a sample prepared by Honeyman and Stening,[9] m. p. 122—123°), $[\alpha]_D^{20}$ +25° (*c*, 0·6 in $CHCl_3$) (Found: C, 51·3; H, 5·9; S, 8·7. $C_{16}H_{22}O_8S$ requires C, 51·3; H, 5·9; S, 8·5%).

Methyl 4 : 6-O-*Ethylidene*-2-O-*methyl*-α-D-*mannoside* 3-*Toluene*-p-*sulphonate* (II).—The 3-toluene-*p*-sulphonate (I) (1 g.) was dissolved in boiling methyl iodide (5 ml.), and silver oxide (1·5 g.) was added during 5 hr.; heating was continued for a further 19 hr. The silver residues were filtered off and washed with chloroform. Evaporation of the filtrate afforded *methyl* 4 : 6-O-*ethylidene*-2-O-*methyl*-α-D-*mannoside* 3-*toluene*-p-*sulphonate* (II) (0·8 g.), m. p. 149—150° (from methanol), $[\alpha]_D^{18}$ +22° (*c*, 0·6 in $CHCl_3$) (Found: C, 51·9; H, 5·8; S, 7·9. $C_{17}H_{24}O_8S$ requires C, 52·5; H, 6·2; S, 8·0%).

Methyl 4 : 6-O-*Ethylidene*-2-O-*methyl*-α-D-*mannoside* (III).—Methyl 4 : 6-*O*-ethylidene-2-*O*-methyl-α-D-mannoside 3-toluene-*p*-sulphonate (0·7 g.) was dissolved in methanol–water (9 : 1; 25 ml.), sodium amalgam (4%; 10 g.) was added, and the mixture was stirred at 45° for 4 hr. and at room temp. for 20 hr. After being decanted from mercury the solution was neutralised with carbon dioxide, inorganic salts were filtered off, and the filtrate was evaporated. The

[13] Newth, *J.*, 1956, 441.

residue was extracted with chloroform; evaporation gave a syrup which crystallised from ether–light petroleum to yield *methyl* 4 : 6-O-*ethylidene*-2-O-*methyl*-α-D-*mannoside* (III) (0·3 g.), m. p. 76—77°, $[\alpha]_D^{19}$ +42° (*c*, 0·6 in $CHCl_3$) (Found : C, 52·0; H, 7·6; OMe, 25·8. $C_{10}H_{18}O_6$ requires C, 51·3; H, 7·7%; OMe, 26·3%).

2-O-*Methyl*-α-D-*mannose* (IV).—Methyl 4 : 6-*O*-ethylidene-2-*O*-methyl-α-D-mannoside (1·6 g.) was heated with 0·5N-hydrochloric acid (25 ml.) at 100° for 6 hr. (constant rotation). The solution was neutralised with silver carbonate and filtered, hydrogen sulphide was passed through the filtrate, and the mixture concentrated. The residue was extracted with boiling ethanol from which the sugar slowly crystallised in a desiccator ($CaCl_2$). 2-*O*-Methyl-α-D-mannose (IV) (0·8 g.) (from ethanol) had m. p. 137°, $[\alpha]_D^{19}$ +15° ⟶ +5° (24 hr., constant) (*c*, 1·3 in H_2O), R_G 0·32 in solvent *a* (Found : C, 42·9; H, 7·2; OMe, 16·3. Calc. for $C_7H_{14}O_6$: C, 43·2; H, 7·2; OMe, 16·0%) {Pacsu and Trister [2] give m. p. 136—137°, $[\alpha]_D$ +7·0° ⟶ +4·5° (H_2O)}. The phenylhydrazone had m. p. 163—164° (Pacsu and Trister [2] record m. p. 163°) (Found : OMe, 11·3. Calc. for $C_{13}H_{20}O_5N_2$: OMe, 10·9%). The syrupy mixture of methyl pyranosides, prepared by refluxing the sugar with dry methanolic hydrogen chloride, consumed 1·01 mol. of periodate at 35° in 8 hr. (spectrophotometric determination [14] carried out by Mr. R. J. Ferrier).

Methyl 4 : 6-O-*Ethylidene*-α-D-*mannoside* 3-*Nitrate* (V).—Ice-cold fuming nitric acid (1·5 ml.) in acetic anhydride (3·5 ml.) was added to a suspension of methyl 4 : 6-*O*-ethylidene-α-D-mannoside (1·5 g.) in acetic anhydride (3·5 ml.) at 0°. After 5 min. at 0° the mixture was poured into ice-water (50 ml.) and the aqueous layer was decanted from the syrupy 2 : 3-dinitrate, neutralised with sodium carbonate, and extracted with chloroform (5 × 50 ml.). Concentration of the extract and two crystallisations of the residue from light petroleum–chloroform yielded *methyl* 4 : 6-O-*ethylidene*-α-D-*mannoside* 3-*nitrate* (V) (0·6 g.), m. p. 166° and mixed m. p. 165° (with a sample prepared by Honeyman and Stening,[9] m. p. 165°), $[\alpha]_D^{20}$ +57° (*c*, 0·9 in $CHCl_3$) (Found : C, 40·6; H, 5·7; N, 5·3. $C_9H_{15}O_8N$ requires C, 40·7; H, 5·7; N, 5·3%).

Methyl 4 : 6-O-*Ethylidene*-2-O-*methyl*-α-D-*mannoside* 3-*Nitrate* (VI).—Silver oxide (3 g.) was added portionwise during 5 hr. to a suspension of the 3-nitrate (V) (3 g.) in boiling methyl iodide (12 ml.), and the mixture was refluxed for a further 20 hr. The silver residues were washed with hot methanol. The combined washings and filtrate were concentrated to give a syrup which crystallised from light petroleum to yield *methyl* 4 : 6-O-*ethylidene*-2-O-*methyl*-α-D-*mannoside* 3-*nitrate* (VI) (2·6 g.), m. p. 100—101° and mixed m. p. 101° (with a sample prepared by Honeyman and Stening,[9] m. p. 101—102°), $[\alpha]_D^{21}$ +45° (*c*, 1·1 in $CHCl_3$) (Found : C, 43·6; H, 6·2; N, 4·6; OMe, 22·0. $C_{10}H_{17}O_8N$ requires C, 43·0; H, 6·1; N, 5·0; OMe, 22·0).

Denitration of Methyl 4 : 6-O-*Ethylidene*-2-O-*methyl*-α-D-*mannoside* 3-*Nitrate*.—A mixture of iron and zinc dust was added portionwise to methyl 4 : 6-*O*-ethylidene-2-*O*-methyl-α-D-mannoside 3-nitrate (2·5 g.) in acetic acid (50 ml.) at 45°. When reaction started the solution was cooled and kept at room temperature for 15 min. (negative diphenylamine–sulphuric acid test). The filtrate and chloroform washings were combined and washed with water, and the chloroform layer was dried (K_2CO_3) and concentrated. The resulting syrup afforded methyl 4 : 6-*O*-ethylidene-2-*O*-methyl-α-D-mannoside (III) (1·9 g.) (from ether–light petroleum), m. p. and mixed m. p. 78—79°, $[\alpha]_D^{20}$ +42° (*c*, 1·2 in $CHCl_3$) (Found : C, 51·1; H, 7·4; OMe, 26·5. Calc. for $C_{10}H_{18}O_6$: C, 51·3; H, 7·7; OMe, 26·3%).

Methyl 4 : 6-O-*Ethylidene*-α-D-*mannoside* 3-*Nitrate* 2-*Toluene*-p-*sulphonate* (VII).—Toluene-*p*-sulphonyl chloride (5·5 g.) in pyridine (10 ml.) was added to a solution of the 3-nitrate (V) (5 g.) in pyridine (10 ml.) at 0°, and the solution kept for 5 days at room temperature. Water was added and, after standing overnight, the solution was extracted with chloroform. The extract was washed with dilute sulphuric acid, and concentrated to a syrup which yielded *methyl* 4 : 6-O-*ethylidene*-α-D-*mannoside* 3-*nitrate* 2-*toluene*-p-*sulphonate* (VII) (5·7 g.) (from methanol), m. p. 123—124° and mixed m. p. 121—123° (with a sample prepared by Honeyman and Stening,[9] m. p. 121—122°), $[\alpha]_D^{19}$ −12° (*c*, 0·8 in $CHCl_3$) (Found : C, 45·9; H, 4·7; N, 3·1. $C_{16}H_{21}O_{10}NS$ requires C, 45·8; H, 5·0; N, 2·8%).

Methyl 4 : 6-O-*Ethylidene*-α-D-*mannoside* 2-*Toluene*-p-*sulphonate* (VIII).—A mixture of iron and zinc dust was added portionwise to a solution of the 3-nitrate 2-toluene-*p*-sulphonate (VII) (5·5 g.) in acetic acid (110 ml.) and after 15 min. (negative diphenylamine–sulphuric acid

[14] Aspinall and Ferrier, unpublished results.

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test) the solid was filtered off and washed with chloroform. The combined filtrate and washings were washed with water, and the chloroform layer was dried (K_2CO_3) and evaporated to a syrup which afforded *methyl* 4 : 6-O-*ethylidene*-α-D-*mannoside* 2-*toluene*-p-*sulphonate* (VIII) (4·2 g.) (from methanol), m. p. 165—166°, $[\alpha]_D^{17}$ +10° (*c*, 1·5 in $CHCl_3$) (Found: C, 50·8; H, 5·9; S, 8·0. $C_{16}H_{22}O_8S$ requires C, 51·3; H, 5·9; S, 8·5%).

Methyl 4 : 6-O-*Ethylidene*-3-O-*methyl*-α-D-*mannoside* 2-*Toluene*-p-*sulphonate* (IX).—Silver oxide (4 × 3 g.) was added to a suspension of the 2-toluene-*p*-sulphonate (VIII) (4 g.) in boiling methyl iodide (15 ml.) during 24 hr., and heating was continued for a further 16 hr. The silver residues were filtered off and washed with chloroform; evaporation gave a syrup which yielded *methyl* 4 : 6-O-*ethylidene*-3-O-*methyl*-α-D-*mannoside* 2-*toluene*-p-*sulphonate* (IX) (3·9 g.) (from light petroleum), m. p. 131°, $[\alpha]_D^{21}$ −16° (*c*, 0·8 in $CHCl_3$) (Found: C, 52·4; H, 6·4; OMe, 8·1. $C_{17}H_{24}O_8S$ requires C, 52·5; H, 6·2; OMe, 8·0%).

3-O-*Methyl*-α-D-*mannose* (X).—Sodium amalgam (4%; 20 g.) was added to methyl 4 : 6-*O*-ethylidene-3-*O*-methyl-α-D-mannoside 2-toluene-*p*-sulphonate (1·7 g.) in methanol–water (9 : 1; 35 ml.), and the mixture was stirred at 45° for 4 hr. and at room temperature for 20 hr. After the solution had been decanted from mercury it was neutralised with carbon dioxide, inorganic salts were filtered off, and the filtrate was evaporated. The residue was extracted with chloroform, and concentration yielded a syrup (0·8 g.; presumably methyl 4 : 6-*O*-ethylidene-3-*O*-methyl-α-D-mannoside). This was heated with 0·5N-hydrochloric acid (15 ml.) at 100° for 5·5 hr. (constant rotation), and the solution was neutralised with silver carbonate. The filtrate was treated with Amberlite resin IR-120(H) and concentrated to a syrup which crystallised from methanol to give 3-O-*methyl*-α-D-*mannose* (X) (0·35 g.), m. p. 133—134° (from ethanol–ether), $[\alpha]_D^{19}$ +14° ⟶ +3° (±1°) (24 hr., constant) (*c*, 0·6 in H_2O) (Found: C, 43·2; H, 6·5; OMe, 16·1. $C_7H_{14}O_6$ requires C, 43·2; H, 7·2; OMe, 16·0%). A mixture with 2-*O*-methyl-α-D-mannose had m. p. 110—125°. The sugar had a similar R_G 0·30 in solvent *a* to the 2-methyl ether, but travelled more slowly ($R_{mannose}$ 1·9) than the 2-methyl ether ($R_{mannose}$ 2·1) in solvent *b*. When heated with phenylhydrazine acetate the sugar (X) gave 3-*O*-methyl-D-glucosazone, m. p. 165—166° which gave an *X*-ray powder photograph identical with that given by an authentic sample. The derived syrupy mixture of methyl pyranosides (prepared by refluxing the sugar with dry methanolic hydrogen chloride) consumed 0·0 mol. of sodium metaperiodate solution during 8 hr. at 35°.

Preparation of 1 : 6-*Anhydro*-4-O-*methyl*-β-D-*mannopyranose*.—Finely ground ivory nuts (400 g.) were pyrolysed as described by Knauf, Hann, and Hudson.[15] The dark distillate was neutralised with barium carbonate and treated with charcoal–Celite. Evaporation yielded a thick syrup which was dissolved in acetone (500 ml.) and shaken with concentrated sulphuric acid (3 ml.) for 48 hr. After neutralisation with cupric carbonate the filtrate was concentrated to a syrup which crystallised on addition of propan-2-ol, and after recrystallisation from the same solvent gave 1 : 6-anhydro-2 : 3-*O*-*iso*propylidene-β-D-mannopyranose (20 g.), m. p. 161—162°, $[\alpha]_D^{19}$ −57° (*c*, 1·2 in H_2O).

Methylation acording to the method of Knauf *et al.*[15] gave a product which was dissolved in benzene and chromatographed on alumina (*b*). Elution with ether–light petroleum (b. p. 40—60°) afforded a syrup which crystallised from the same solvent to give 1 : 6-anhydro-4-*O*-methyl-2 : 3-*O*-*iso*propylidene-β-D-mannopyranose (16 g.), m. p. 52—53°, $[\alpha]_D^{19}$ −33° (*c*, 0·7 in $CHCl_3$).

Hydrolysis of the *iso*propylidene compound gave syrupy 1 : 6-anhydro-4-*O*-methyl-β-D-mannopyranose (Found: OMe, 18·0. Calc. for $C_7H_{12}O_5$: OMe, 17·6%).

1 : 6-*Anhydro*-4-O-*methyl*-β-D-*mannopyranose* 2-*Toluene*-p-*sulphonate* (XI).—Toluene-*p*-sulphonyl chloride (4·6 g.) in pyridine (25 ml.) was added to 1 : 6-anhydro-4-*O*-methyl-β-D-mannopyranose (4 g.) in pyridine (25 ml.) at 0°. The mixture was kept for 48 hr. at −5° and then for 24 hr. at 0°. The solution was poured into sodium hydrogen carbonate solution, the mixture evaporated to remove most of the pyridine, the residue extracted with chloroform, and the extract washed with dilute sulphuric acid, sodium hydrogen carbonate solution, and water. Concentration gave a syrup which when crystallised from acetone–ether had m. p. 84—86°. This crystalline substance (5·1 g.) was dissolved in benzene and chromatographed on alumina (*b*). Elution with benzene–ether afforded 1 : 6-*anhydro*-4-O-(*ethyl*-β-D-*mannopyranose* 2-*toluene*-p-*sulphonate* (XI), m. p. 85—87°, $[\alpha]_D^{20}$ −42° (*c*, 1·0 in $CHCl_3$) (Found: C, 51·0; H, 5·4; S, 9·4; OMe, 9·0. $C_{14}H_{18}O_7S$ requires C, 50·9; H, 5·5; S, 9·7; OMe, 9·4%); elution with

[15] Knauf, Hann, and Hudson, *J. Amer. Chem. Soc.*, 1941, **63**, 1447.

ether and acetone–ether yielded further small quantities of the same compound but no other substance could be detected.

1 : 6-*Anhydro*-3 : 4-*di*-O-*methyl*-β-D-*mannopyranose* 2-*Toluene*-p-*sulphonate (XII).—The 2-toluene-*p*-sulphonate (XI) (4 g.) was dissolved in acetone (8 ml.), and methyl iodide (8 ml.) and anhydrous calcium sulphate (5 g.) were added. Silver oxide (3 × 5 g.) was added during 3 hr. to the boiling solution and heating was continued for a further 13 hr. The solid was filtered off and extracted with hot acetone; evaporation gave a syrup which crystallised from acetone–ether. This product (3·5 g.; m. p. 96—100°) was dissolved in benzene and chromatographed on alumina (*b*). Elution with benzene–light petroleum gave a syrup which crystallised from ether to yield **1 : 6-*anhydro*-3 : 4-*di*-O-*methyl*-β-D-*mannopyranose* 2-*toluene*-p-*sulphonate** (XII) (1·8 g.), m. p. 88—89°, $[\alpha]_D^{19}$ −35° (*c*, 1·0 in $CHCl_3$) (Found: C, 52·4; H, 5·5; S, 9·2; OMe, 18·1. $C_{15}H_{20}O_7S$ requires C, 52·3; H, 5·9; S, 9·3; OMe, 18·0%). Elution with ether and acetone–ether gave unchanged starting material (XI) (1·7 g.), m. p. and mixed m. p. 85—87° (from ether); this material was suspended in boiling methyl iodide (5 ml.) and silver oxide (7 g.) was added during 12 hr. The product was worked up in the usual way and chromatographed on alumina (*b*) to give more of the dimethyl ether (XII) (1·4 g.), m. p. and mixed m. p. 87—89°.

1 : 6-*Anhydro*-β-D-*mannopyranose* 2-*Toluene*-p-*sulphonate* (XIII).—1 : 6-Anhydro-β-D-mannopyranose (prepared by the hydrolysis of 1 : 6-anhydro-2 : 3-*O*-*iso*propylidene-β-D-mannopyranose) (3 g.) was dissolved in pyridine (20 ml.) at 0° and a solution of toluene-*p*-sulphonyl chloride (2·5 g.) in pyridine (20 ml.) at 0° was added. The mixture was kept at −5° for 48 hr. and then at 0° for 24 hr. Water (2 ml.) was added and the mixture was poured into water (50 ml.) containing sodium hydrogen carbonate (3 g.). The aqueous layer was decanted from the small quantity of syrup which separated and the solution was concentrated (more syrup separated during the evaporation). The residue was extracted with acetone and the extract concentrated; addition of water gave **1 : 6-*anhydro*-β-D-*mannopyranose* 2-*toluene*-p-*sulphonate*** (XIII) (2·9 g.), m. p. 146—147° (after recrystallisation from acetone–ether), $[\alpha]_D^{19}$ −74° (*c*, 0·5 in $COMe_2$) (Found: C, 49·3; H, 5·2. $C_{13}H_{16}O_7S$ requires C, 49·4; H, 5·1%).

Methylation of **1 : 6-*Anhydro*-β-D-*mannopyranose* 2-*Toluene*-p-*sulphonate***.—1 : 6-Anhydro-β-D-mannopyranose 2-toluene-*p*-sulphonate (2·5 g.) was dissolved in acetone (5 ml.), and methyl iodide (8 ml.) and anhydrous calcium sulphate (4 g.) were added. Silver oxide (5 × 3 g.) was added during 5 hr. to the boiling solution and heating was continued for a further 7 hr. After being worked up in the usual way the syrup was dissolved in benzene and chromatographed on alumina (*b*). Elution with benzene–light petroleum and crystallisation from ether gave the 3 : 4-dimethyl ether (XII) (1·1 g.), m. p. and mixed m. p. 87—88°. Elution with benzene–ether and crystallisation from ether gave the 4-methyl ether (XI) (1·0 g.), m. p. and mixed m. p. 85—87°. Remethylation of the 4-methyl ether (XI) with methyl iodide and silver oxide followed by chromatography on alumina (*b*) afforded the 3 : 4-dimethyl ether (XII) (0·8 g.), m. p. and mixed m. p. 86—87°.

1 : 6-*Anhydro*-3 : 4-*di*-O-*methyl*-β-D-*mannopyranose* (XIV).—1 : 6-Anhydro-3 : 4-di-*O*-methyl-β-D-mannopyranose 2-toluene-*p*-sulphonate (1·8 g.) was dissolved in methanol–water (9 : 1; 35 ml.), and sodium amalgam (4%; 35 g.) was added. The mixture was stirred at 40° for 4 hr. and at room temperature overnight. The solution and methanol washings were decanted from the mercury and neutralised with carbon dioxide; inorganic salts were filtered off and the filtrate was concentrated. The residue was extracted with chloroform, and the extract evaporated to a syrup which was crystallised from acetone–ether and then from light petroleum–ether. **1 : 6-*Anhydro*-3 : 4-*di*-O-*methyl*-β-D-*mannopyranose*** (XIV) (0·85 g.) had m. p. 63—65°, $[\alpha]_D^{20}$ −90° (*c*, 0·6 in $CHCl_3$) (Found: C, 50·7; H, 7·2; OMe, 31·8. $C_8H_{14}O_5$ requires C, 50·5; H, 7·4; OMe, 32·6%).

3 : 4-*Di*-O-*methyl*-D-*mannose* (XV).—1 : 6-Anhydro-3 : 4-di-*O*-methyl-β-D-mannopyranose (0·8 g.) was heated with N-hydrochloric acid (30 ml.) at 100° for 110 min. (constant rotation), and the solution was neutralised with silver carbonate and filtered. Hydrogen sulphide was passed through the solution, the mixture was taken to dryness, and the residue extracted with methanol yielding a solution from which 3 : 4-di-*O*-methyl-α-D-mannose monohydrate, m. p. 109—111°, crystallised. The sugar slowly changed to a more stable crystalline form, m. p. 78—80°. After recrystallisation from acetone–ether the sugar had m. p. 78—80° and mixed m. p. 78—81° (with an authentic sample, m. p. 80—82°), $[\alpha]_D^{19}$ +18° (4 min.) ⟶ +6° (24 hr., constant) (Found: C, 42·2; H, 8·0; OMe, 27·2. Calc. for $C_8H_{16}O_7$: C, 42·5; H, 8·0; OMe,

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27·2%). The sugar had R_g 0·67 in solvent *a*, and on oxidation with bromine gave 3 : 4-di-*O*-methyl-D-mannonolactone, m. p. 159—160° and mixed m. p. 159—161° (with an authentic sample, m. p. 161—162°), $[\alpha]_D^{19}$ +178° (20 min.) ⟶ +132° (68 hr., constant) (*c*, 0·56 in H_2O).

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437. *Sugar Nitrates. Part III.* Mannose Derivatives.*

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Methyl 4 : 6-*O*-ethylidene-α-D-mannoside 2 : 3-dinitrate reacts with sodium methoxide, sodium iodide, and sodium nitrite in the same way as the corresponding D-glucose derivative; the ester group on $C_{(2)}$ is converted into the alcohol more readily than that on $C_{(3)}$.

The 2 : 3-ditoluene-*p*-sulphonate is more stable towards sodium methoxide than the D-glucose analogue, but the 3-toluene-*p*-sulphonate may be obtained by treatment of the ditoluene-*p*-sulphonate with this reagent.

As in the analogous glucose compound the nitrate group on $C_{(2)}$ of methyl 4 : 6-*O*-ethylidene-α-D-mannoside 2 : 3-dinitrate [1] is preferentially removed (yielding the alcohol) by reaction with sodium methoxide in cold methanol–chloroform, or by sodium iodide in acetone at 100°, or, best, by sodium nitrite in boiling aqueous ethanol. The action of sodium methoxide on the D-glucoside 2 : 3-dinitrate in which the nitrate groups are *trans* and equatorial in the preferred conformation yields the parent D-glucoside and the 2 : 3-anhydro-α-D-alloside. In the D-mannoside derivative the nitrate groups and their attached carbon atoms cannot become coplanar in any conformation. Newth [2] has pointed out, however, that coplanarity, favourable for an intramolecular S_N2 process resulting in epoxide formation, is possible for esters of methyl 4 : 6-*O*-benzylidene-α-D-glucoside. This accounts for the formation of an anhydro-compound from the D-glucose dinitrate and for the absence of such an epoxide during the present work on D-mannose.

Methyl 4 : 6-*O*-ethylidene-α-D-mannoside 2 : 3-ditoluene-*p*-sulphonate is converted by sodium methoxide into the 3-toluene-*p*-sulphonate rather more slowly than is the glucose derivative.

The products obtained are similarly substituted whether the starting compounds are glucose derivatives in which substituents on both $C_{(2)}$ and $C_{(3)}$ are equatorial or mannose where the one on $C_{(2)}$ is axial and the other equatorial. The enhanced reactivity of the group on $C_{(2)}$ does not, therefore, appear to arise from purely steric considerations such as greater accessibility. Electronic effects transmitted from the neighbouring methoxyl group or ring oxygen may be of importance.[3]

The characterization of the new compounds described has been achieved by establishing their identity with those obtained simultaneously but independently by Aspinall and Zweifel.[4]

EXPERIMENTAL

Chloroform solutions were dried over sodium sulphate before being evaporated under reduced pressure. The light petroleum used had b. p. 60—80°.

* Part II, *J.*, 1955, 3660.

[1] Honeyman and Morgan, *J.*, 1954, 744.
[2] Newth, *J.*, 1956, 441.
[3] Sugihara, *Adv. Carbohydrate Chem.*, 1953, **8**, 1.
[4] Aspinall and Zweifel, preceding paper.

Chromatographic separations were carried out with columns of activated alumina, Type H, 100/200S mesh, supplied by Messrs. Peter Spence and Sons Ltd.

Alkaline Hydrolysis of Methyl 4 : 6-O-*Ethylidene*-α-D-*mannoside* 2 : 3-*Dinitrate*.—After being kept for 6 weeks at 0° a solution of methyl 4 : 6-*O*-ethylidene-α-D-mannoside 2 : 3-dinitrate [1] (2 g.) in chloroform (24 ml.) and methanol (13 ml.) containing sodium (0·74 g.) was neutralized with glacial acetic acid. The residue obtained by evaporating the solution was dissolved in benzene, filtered, and chromatographed. Elution with benzene yielded *methyl* 4 : 6-O-*ethylidene*-α-D-*mannoside* 2-*nitrate* (6%), m. p. 125° after several recrystallizations from ether–light petroleum (Found : C, 41·0; H, 5·8. $C_9H_{15}O_8N$ requires C, 40·8; H, 5·7%). Further elution with chloroform removed methyl 4 : 6-*O*-ethylidene-α-D-mannoside 3-nitrate (29%), m. p. 165° (unaltered after admixture with Aspinall and Zweifel's preparation, m. p. 166°), $[\alpha]_D^{19}$ +51·3° (*c* 0·7 in $CHCl_3$), after recrystallization from ether–light petroleum (Found : C, 40·6; H, 5·7%). A final extraction of the column with methanol gave methyl 4 : 6-*O*-ethylidene-α-D-mannoside (20%), m. p. 115°, undepressed after admixture with authentic compound.

A solution similar to the above was badly coloured after 10 minutes' boiling. The products isolated were methyl 4 : 6-*O*-ethylidene-α-D-mannoside (15%) and its 3-nitrate (4%).

Alkaline Hydrolysis of Methyl 4 : 6-O-*Ethylidene*-α-D-*mannoside* 2 : 3-*Ditoluene*-p-*sulphonate*.—A solution of this 2 : 3-ditoluene-*p*-sulphonate [1] (1·5 g.) in chloroform (18 ml.) and methanol (5·6 ml.) containing sodium (0·33 g.) was kept at 0° for 6 weeks. Neutralization with glacial acetic acid followed by evaporation gave a solid residue which was chromatographed in benzene. Elution with benzene gave unchanged starting compound (41%); further elution with chloroform yielded a solid which, after recrystallization from ether–light petroleum, was methyl 4 : 6-*O*-ethylidene-α-D-mannoside 3-toluene-*p*-sulphonate (24%), m. p. 122—123° raised to 125° by admixture with Aspinall and Zweifel's compound of m. p. 129° (Found : C, 51·3; H, 5·8. Calc. for $C_{16}H_{22}O_8S$: C, 51·3; H, 5·9%).

Preparation of Methyl 4 : 6-O-*Ethylidene*-α-D-*mannoside* 3-*Nitrate and its* 2-*Toluene*-p-*sulphonate*.—(1) The 2 : 3-dinitrate (3 g.) and sodium iodide (6 g.) in acetone (25 ml.) were kept at 100° in a sealed tube for a day. The chloroform extract of the evaporated solution was washed with aqueous sodium thiosulphate and then chromatographed. Elution with chloroform removed methyl 4 : 6-*O*-ethylidene-α-D-mannoside 3-nitrate (34%), m. p. 165—166° after recrystallization. Further extraction of the column with methanol gave methyl 4 : 6-*O*-ethylidene-α-D-mannoside (23%).

Under these conditions the corresponding 2 : 3-ditoluene-*p*-sulphonate was recovered unchanged (90%).

(2) A solution of the 2 : 3-dinitrate (2·8 g.) and sodium nitrite (1·8 g.) in ethanol (20 ml.) and water (5 ml.) was boiled under reflux for 20 hr. before the solvents were evaporated. The chloroform extract of the residue was evaporated to a syrup which was dissolved in benzene and chromatographed. Elution with benzene yielded starting compound (16%); further elution with chloroform afforded the 3-nitrate (58%).

The 3-nitrate (0·48 g.), toluene-*p*-sulphonyl chloride (0·5 g.), and pyridine (4 ml.) were mixed at 0° and after 4 days at room temperature poured into water. Recrystallization of the resulting solid from ethanol–light petroleum led to methyl 4 : 6-*O*-ethylidene-α-D-mannoside 3-nitrate 2-toluene-*p*-sulphonate (83%), m. p. 121—122° (undepressed after admixture with Aspinall and Zweifel's compound, m. p. 123—124°), $[\alpha]_D^{21}$ −17·0° (*c* 0·2 in $CHCl_3$) (Found : C, 46·0; H, 5·2. Calc. for $C_{16}H_{21}O_{10}NS$: C, 45·8; H, 5·0%).

Preparation of Methyl 2-O-*Methyl*-α-D-*mannoside* 3-*Nitrate*.—Silver oxide (3 g.) was added during 5 hr. to methyl iodide (20 ml.) boiling under reflux and containing methyl 4 : 6-*O*-ethylidene-α-D-mannoside 3-nitrate (1 g.). After being boiled for 19 hr. more the mixture was filtered and evaporated. The white solid obtained by extraction of the residue with chloroform was, after recrystallization from light petroleum, methyl 4 : 6-*O*-ethylidene-2-*O*-methyl-α-D-mannoside 3-nitrate (70%), m. p. 101—102° (unchanged on admixture with Aspinall and Zweifel's compound, m. p. 100—101°), $[\alpha]_D^{21}$ +43·8° (*c* 0·9 in $CHCl_3$) (Found : C, 43·2; H, 6·0. Calc. for $C_{10}H_{17}O_8N$: C, 43·0; H, 6·1%).

A suspension of this compound (0·85 g.) in acetone (10 ml.) and water (5 ml.) containing sulphuric acid (0·55 ml.) was boiled under reflux for 13 hr. After neutralization with barium hydroxide the mixture was evaporated and the residue extracted with chloroform. Evaporation left a syrup which was chromatographed in benzene solution. Elution with benzene and

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with chloroform removed impurities and elution with methanol gave *methyl 2-O-methyl-α-D-mannoside 3-nitrate* (51%), m. p. 98°, $[\alpha]_D^{19}$ +43·9° (*c* 1·0 in $CHCl_3$) (Found: C, 38·0; H, 6·0. $C_8H_{15}O_8N$ requires C, 38·0; H, 6·0%).

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438. *Wool Wax. Part VII.* The Autoxidation of Dihydrolanosteryl Acetate.*

By D. H. S. HORN and D. ILSE.

On autoxidation, dihydrolanosteryl acetate (I) yielded the 7β-hydroperoxy-† and 7β : 11α-dihydroperoxy-derivatives† (III) and (II), together with smaller quantities of 7-oxo- and 7 : 11-dioxo-derivatives (VIII) and (V). The 7β-hydroperoxide (III) was decomposed by aqueous ferrous ammonium sulphate into the 7-oxo-, 7β-hydroxy-,† and 7 : 9-diene-derivatives (VIII), (IV), and (VII), respectively.

IN earlier communications [1] it was shown that commercial wool wax contains a complex group of largely unidentified substances which are autoxidation products of cholesterol, lanosterol, and dihydrolanosterol. The structures of the major primary autoxidation products of cholesterol have been elucidated,[2] principally by Bergström and Wintersteiner,[3] and some of these characteristic autoxidation products, absent in significant quantities from freshly secreted wax, have been isolated from the commercial wax by Daniel *et al.*[3] and Milburn *et al.*[4] A study has now been made of the autoxidation of dihydrolanosteryl acetate (I) to assist the identification of some of the remaining wool-wax autoxidation products.

Lanost-8-en-3β-yl acetate (dihydrolanosteryl acetate) in ethyl acetate readily absorbed oxygen at 50°; and, after 48 hours, the peroxide content of the solute, determined by Sully's method,[5] had reached a value of 1·6 milliequiv./g., or 80% hydroperoxide (calculated as $C_{32}H_{54}O_4$). On chromatography on alumina, this material was partly decomposed into 7-oxolanost-8-en-3β-yl acetate (VIII), 7 : 11-dioxolanost-8-en-3β-yl acetate (V), and lanosta-7 : 9-dien-3β-yl acetate (VII) and unidentified resin. Separation of the autoxidation products was effected with the minimum of decomposition by means of countercurrent distribution, or more conveniently by reversed-phase partition chromatography,[6] into two hydroperoxide fractions together with very small quantities of unsaturated ketones.

The second hydroperoxide fraction yielded a pure monoperoxide, whose structure, formulated as (III), was elucidated by the following series of reactions: on catalytic hydrogenation, the hydroperoxide yielded an alcohol (IV), which on mild oxidation with

* Part VI, *J.*, 1954, 1460.

† The infrared spectra of compounds thus marked have been offered for inclusion in the D.M.S. collection (cf. *J.*, 1955, 4501).

[1] Horn and Ilse, *Chem. and Ind.*, 1956, 524; Horn, *Manuf. Chem.*, 1955, No. 4, p. 3.

[2] Bergström and Wintersteiner, *J. Biol. Chem.*, 1941, **141**, 596; 1942, **143**, 503; **145**, 309, 327; Mosbach, Nierenberg, and Kendall, *J. Amer. Chem. Soc.*, 1953, **75**, 2358; Fieser, *Science*, 1954, **119**, 710.

[3] Daniel, Lederer, and Velluz, *Bull. Soc. Chim. biol.*, 1945, **27**, 218.

[4] Milburn, Truter, and Woodford, *J.*, 1956, 1740.

[5] Sully, *Analyst*, 1954, **79**, 86.

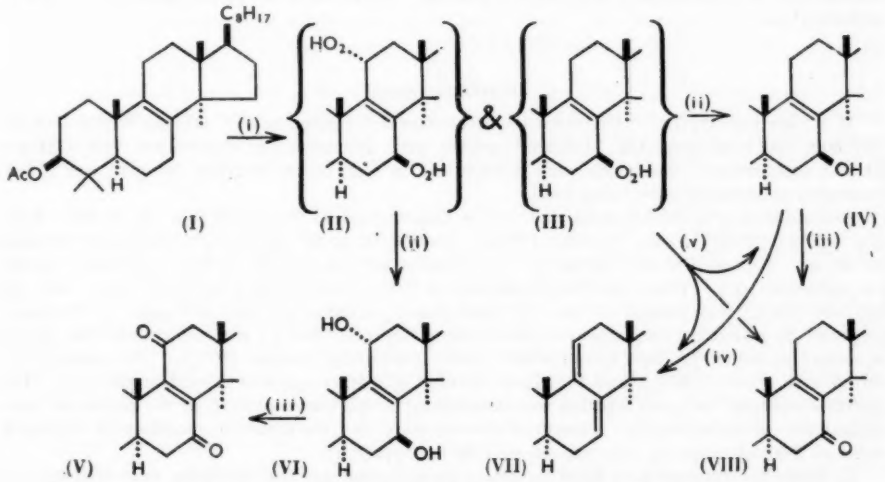
[6] Howard and Martin, *Biochem. J.*, 1950, **46**, 532; Sephton and Sutton, *J. Amer. Oil Chemists' Soc.*, 1956, **33**, 263.

chromic oxide in acetone according to the method of Bowers *et al.*[7] yielded 7-oxolanost-8-en-3β-yl acetate (VIII). Attempted mild acetylation of the alcohol (IV) yielded lanosta-7 : 9-dien-3β-yl acetate (VII).[8]

The 7-hydroxyl group of compound (IV), and hence the 7-hydroperoxyl group of (III), is assigned the β-configuration on the basis of molecular-rotation evidence, the contribution (ΔM_D, in $CHCl_3$) of the 7-hydroxyl group in the 7β-hydroxy-acetate being +97°, those of 7α- and 7β-hydroxycholestane being −59° and +110°, respectively.[9]

In the autoxidation of cholesterol, attack takes place at both 7α- and 7β-positions.[10] The absence of the epimeric 7α-hydroperoxy-derivative or of a 7 : 9-diene in the autoxidation products, suggests that the 7α-position is sufficiently hindered sterically by the 14α-methyl group in the lanost-8-ene series to prevent significant autoxidative attack at the 7α-position.[11]

The hydroperoxide (III) with aqueous ferrous ammonium sulphate gave 7-oxolanost-8-en-3β-yl acetate (VIII), 7-hydroxylanost-8-en-3β-yl acetate (IV), and lanosta-7 : 9-dien-3β-yl acetate (dihydroagnosteryl acetate) (VII). The 7 : 9-dienyl artefacts (esters of agnosterol and dihydroagnosterol) present in autoxidised wool wax, are probably formed by the decomposition of the corresponding 7-hydroperoxides by metal catalysts, particularly manganese salts known to be present in the wax.[12] In view of the ease of formation



(i), O_2. (ii), Pd–H_2. (iii), CrO_3. (iv), Ac_2O. (v), Fe^{++}.

of this heteroannular conjugated diene system on autoxidation, other analogous dienes accompanying naturally occurring lanost-8-enes in small amounts, might also be artefacts (*e.g.*, dehydroburicoic acid).

The first hydroperoxide fraction to be eluted from the column yielded a crystalline dihydroperoxide formulated as (II). On catalytic hydrogenation it gave an acetoxy-diol

[7] Bowers, Halsall, Jones, and Lemin, *J.*, 1953, 2548.
[8] Cf. also Marker, Whittle, and Mixon, *J. Amer. Chem. Soc.*, 1937, **59**, 1368.
[9] Braude and Nachod, "Determination of organic structures by physical methods," Academic Press Inc., New York, 1955, p. 111.
[10] Bergström and Wintersteiner, ref. 2.
[11] Fieser and Fieser, "Organic Chemistry," 3rd edn., Reinhold Publishing Corp., New York, 1956, p. 965.
[12] von Rudloff, "A Study of the Saponifiable and the Unsaponifiable Components of Wool Wax," D.Sc. Thesis, Pretoria Univ., 1952, 80—81, 140—141; Truter and Woodford, *Chem. and Ind.*, 1954, 1323.

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(VI), which was acetylated to a triacetate. Mild chromic oxidation of the acetoxy-diol yielded 7 : 11-dioxolanost-8-en-3β-yl acetate (V), in support of the structure (II) assigned to the dihydroperoxide.

The formation of the 7 : 11-dihydroperoxide is surprising in view of the absence of detectable amounts of the 11-hydroperoxide. However, as the 11-position is less easily attacked than the 7-position, it is possible that at the advanced stages of autoxidation reached, most of the small amount of 11-hydroperoxide formed had been converted into the dihydroperoxide, as the dihydroperoxide should be more rapidly formed from the 11- than the 7-hydroperoxide. Alternatively the 11-position may be activated by a 7-hydroperoxide substituent or by an unstable 7-substituted-radical intermediate.

Too little of the acetoxy-diol (VI) was available for molecular-rotation measurements, but it is reasonable to assume the 7-hydroperoxyl group of the dihydroperoxide to have the β-configuration as hydroperoxide in (III), and following the ready acetylation of the 11-hydroxyl group of the acetoxy-diol (VI) and on steric grounds,[13] the 11-hydroxyl group is assigned the α-configuration.

Besides the hydroperoxides isolated, very small amounts of unsaturated ketones, probably decomposition products of the two hydroperoxides, were present. These ketones were not isolated, but from ultraviolet and infrared absorptions measurements are considered to be 7-oxolanost-8-en-3β-yl acetate (VIII) and 7 : 11-dioxolanost-8-en-3β-yl acetate (V).

Experimental

M. p.s are uncorrected. Ultraviolet spectra were determined in 96% ethanol with a Unicam (S.P.500) spectrophotometer. Infrared spectra were determined in chloroform with a Hilger (H.800) instrument. Rotations were determined in chloroform at room temperature, a 0·5-decimetre polarimeter tube being used.

Autoxidation of Lanost-8-en-3β-yl Acetate.—Lanost-8-en-3β-yl acetate {5 g., m. p. 120—121°, $[\alpha]_D$ +57·3 (*c*, 1·24)} in ethyl acetate (100 ml.) was heated to 50° and oxygen was passed through for 48 hr. Removal of the solvent in a vacuum at 40° gave a solid (5·2 g.; peroxide content 1·6 milliequiv./g.). This material in suspension with non-wetting Supercel [6] (15 g.) and *iso*-heptane (15 g.) was poured on to a reversed-phase partition column (800 mm. × 34 mm.), prepared by pouring a suspension of non-wetting Supercel (240 g.) and *iso*heptane (240 g.), in aqueous ethanol (80%), into an unpacked column containing ethanol (80%). The column was eluted with ethanol (80%), and the eluate divided into fractions with a syphon (36 c.c.). The peroxide content [8] of each fraction was determined and a curve plotted of the peroxide value against the volume of eluate. The curve showed two peaks, the first corresponding to a peroxide value of 2·0 milliequiv./g., the second to 1·25 milliequiv./g.

7β-*Hydroperoxylanost-8-en-3β-yl Acetate.*—Evaporation of the fractions corresponding to the second peroxide maximum gave a residue (2·2 g.) of 7β-*hydroperoxylanost-8-en-3β-yl acetate* as needles (from methanol), m. p. 159—160°, $[\alpha]_D$ +67·4° (*c*, 0·6) (Found: C, 76·4; H, 11·1. $C_{32}H_{54}O_4$ requires C, 76·4; H, 10·8%).

7β-*Hydroxylanost-8-en-3β-yl Acetate.*—Reduction of 7β-hydroperoxylanost-8-en-3β-yl acetate (1·5 g.) in ethanol (300 c.c.; 96%) with hydrogen for 3 hr. in presence of palladium–calcium carbonate catalyst (1·5 g.) gave 7β-*hydroxylanost-8-en-3β-yl acetate* (1·2 g.), flat needles (from methanol), m. p. 163—164°, $[\alpha]_D$ +76·3° (*c*, 1·0) (Found: C, 79·1; H, 11·3. $C_{32}H_{54}O_3$ requires C, 79·0; H, 11·2%).

Attempted Acetylation of 7β-*Hydroxylanost-8-en-3β-yl Acetate.*—The hydroxy-acetate (450 mg.) in acetic anhydride–pyridine (1 : 1; 30 c.c.) was kept overnight at room temperature. After being worked up in the usual way the product was adsorbed from hexane on alumina (20 g.). Elution with hexane–benzene (1 : 1; 100 c.c.) gave a solid (355 mg.), which after one crystallisation gave pure lanosta-7 : 9-dien-3β-yl acetate, $\lambda_{max.}$ 243 mμ (log ε 4·2), m. p. 167—168°, undepressed on admixture with an authentic specimen prepared from wool wax. Further elution with ether gave a yellowish-brown gum (75 mg.).

[13] Fieser and Fieser, *loc. cit.*, p. 979.

7-Oxolanost-8-en-3β-yl Acetate.—7β-Hydroxylanost-8-en-3β-yl acetate (500 mg.) in acetone (200 c.c.) was oxidised with aqueous chromic acid as described by Bowers *et al.*[7] The crude product, in hexane–benzene (1 : 1), was chromatographed on acid-washed alumina and yielded 7-oxolanost-8-en-3β-yl acetate (240 mg.). Recrystallised from ethanol it had $[\alpha]_D$ +21·3° (*c*, 1·0), $\lambda_{max.}$ 253 mμ (log ε 4·06), m. p. 151—152°, undepressed on admixture with an authentic specimen [14] (Found : C, 79·0; H, 10·5. Calc. for $C_{32}H_{52}O_3$: C, 79·3; H, 10·8%).

Decomposition of 7β-Hydroperoxylanost-8-en-3β-yl Acetate with Ferrous Ammonium Sulphate.—The pure hydroperoxide (1·0 g.) in ether–ethanol (1 : 1; 100 c.c.) was shaken overnight with aqueous ferrous ammonium sulphate (5%; 50 c.c.). Extraction of the product with ether gave a yellow glass which was adsorbed from hexane–benzene (1 : 1; 10 c.c.) on to acid-washed alumina (30 g.). Elution with the same solvent and crystallisation from ethanol–ethyl acetate (1 : 1) gave lanosta-7 : 9-dien-3β-yl acetate (309 mg.), $[\alpha]_D$ +90° (*c*, 1·09), $\lambda_{max.}$ 242 mμ (log ε 4·2), m. p. 169° undepressed on admixture with an authentic sample obtained from wool wax (Found : C, 82·1; H, 11·2. Calc. for $C_{32}H_{52}O_2$: C, 82·0; H, 11·2%).

Further elution of the column with benzene gave 7-oxolanost-8-en-3β-yl acetate (174 mg.), which after repeated crystallisation from ethanol had $\lambda_{max.}$ 253 mμ (log ε 4·03), $[\alpha]_D$ +20·5° (*c*, 1·0), m. p. and mixed m. p. 151—151·5° (Found : C, 79·6; H, 10·9. Calc. for $C_{32}H_{52}O_3$: C, 79·3; H, 10·8%).

Elution with ether then gave 7β-hydroxylanost-8-en-3β-yl acetate (251 mg.), m. p. 163° (from methanol) (Found : C, 79·0; H, 10·8. Calc. for $C_{32}H_{54}O_3$: C, 79·0; H, 11·2%).

7β : 11α-Dihydroperoxylanost-8-en-3β-yl Acetate.—Evaporation of the fractions corresponding to the first peroxide maximum gave pale yellow *7β : 11α-dihydroperoxylanost-8-en-3β-yl acetate* (750 mg.), m. p. 210° (from aqueous methanol) (Found : C, 71·5; H, 10·2. $C_{32}H_{54}O_6$ requires C, 71·9; H, 10·2%).

7β : 11α-Dihydroxylanost-8-en-3β-yl Acetate.—Reduction of 7β : 11α-dihydroperoxylanost-8-en-3β-yl acetate (250 mg.) in ethanol (300 c.c.; 96%) with hydrogen for 3 hr. in the presence of palladium–calcium carbonate (250 mg.) gave *7β : 11α-dihydroxylanost-8-en-3β-yl acetate* (240 mg.), m. p. 234° (*in vacuo*) (from methanol) (Found : C, 76·5; H, 11·0. $C_{32}H_{54}O_4$ requires C, 76·4; H, 10·8%).

3β : 7β : 11α-Triacetoxylanost-8-ene.—7β : 11α-Dihydroxylanost-8-en-3β-yl acetate (54 mg.) and acetic anhydride–pyridine (1 : 1, 10 c.c.) at 45° for 15 hr. gave a yellow glass, which on recrystallisation from methanol yielded *3β : 7β : 11α-triacetoxylanost-8-ene*, m. p. 192—193° (Found : C, 73·6; H, 9·9. $C_{36}H_{58}O_6$ requires C, 73·7; H, 10·0%).

Oxidation of 7β : 11α-Dihydroxylanost-8-en-3β-yl Acetate.—7β : 11α-Dihydroxylanost-8-en-3β-yl acetate (324 mg.) in pyridine (4·25 c.c.) was added to chromic oxide (425 mg.)–pyridine (4·25 c.c.). After being kept overnight at room temperature, the mixture was diluted with water and extracted with ether. Evaporation gave a yellow glass, which was adsorbed from benzene on alumina (50 g.). Elution with benzene and crystallisation of the residue (40 mg.) from ethanol gave 7 : 11-dioxolanost-8-en-3β-yl acetate, $\lambda_{max.}$ 270 mμ (log ε 3·98), m. p. 156°, undepressed on admixture with an authentic specimen.[14]

Elution with benzene–ether (1 : 1) then gave unchanged 7β : 11α-dihydroxylanost-8-en-3β-yl acetate (98 mg.) and elution with ether, a yellow resin (80 mg.).

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National Chemical Research Laboratory, South African Council for Scientific and Industrial Research, Pretoria, South Africa. [*Received, December 31st*, 1956.]

[14] Ruzicka, Rey, and Muhr, *Helv. Chim. Acta*, 1944, **27**, 472.

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439. *E.m.f. Measurements in Ethyl Methyl Ketone–Water Mixtures with the Cell* $H_2(Pt)|HCl|AgCl–Ag$. *With an Appendix on Triethylene Glycol–Water Systems.*

By D. Feakins and C. M. French.

Standard potentials of the cell $H_2(Pt)|HCl|AgCl–Ag$ in 10% and 20% ethyl methyl ketone solutions in water are recorded. As with acetone solutions,[1] reversible and reproducible hydrogen-electrode potentials were unobtainable with platinum-black electrodes, but completely satisfactory results were obtained with unplatinised electrodes.[1,2] E.m.f. measurements in the same cell with aqueous solutions of triethylene glycol were not entirely satisfactory, but in view of certain features of interest the results are recorded and discussed briefly in the Appendix.

Measurements of e.m.f. in the cell $H_2(Pt)|HCl|AgCl–Ag$ in aqueous acetone solutions have been reported.[1] These are now extended to solutions of 10 and 20% (w/w) of ethyl methyl ketone in water, and the results, including the standard potentials of this cell in these solvents, recorded.

Certain features in the behaviour of glucose solutions,[3] and to some extent glycerol [4,5,6] and fructose [7] solutions, led us to attempt e.m.f. measurements in triethylene glycol solutions to see whether these features were general for solutions where the organic constituent is of relatively high molecular weight. The results of this work are also reported.

Experimental

Cell measurements (at 25°), preparation of electrodes, and the measurement of vapour pressures and densities were as described earlier.[1] The dielectric constants of the pure solvent mixtures were determined with a radiofrequency bridge.

B.D.H. " Laboratory Reagent " ethyl methyl ketone was shaken with saturated potassium carbonate solution to remove acids,[8] separated, and dried (ignited K_2CO_3, then ignited Na_2SO_4). It was then fractionated 2 or 3 times with rejection of substantial head (containing aldehydes) and tail fractions. The final product only slowly restored the colour to Schiff's reagent: n_D^{20} 1·3785 (lit.,[9] n_D^{20} 1·37850), d_4^{20} 0·8054 (lit.,[10] d_4^{20} 0·8053), b. p. 79·6°/760 mm. (lit.,[11] 79·6°).

Triethylene glycol (B.D.H.) was dried ($CaSO_4$) for one week, and then repeatedly and very slowly distilled at 0·2—0·5 mm. with rejection of substantial head and tail fractions. The colourless liquid thus obtained was stored in a vacuum desiccator over P_2O_5 which was changed every time the desiccator was opened. Care was taken throughout to minimise contact of the liquid with moist air: n_D^{15} 1·4574 (lit.,[12] n_D^{15} 1·4578), d_4^{15} 1·1274 (lit.,[12] d_4^{15} 1·1274), b. p. 120—122°/0·5 mm. (lit.,[11] 115—117°/0·1 mm.).

Discussion of Ethyl Methyl Ketone Systems.—The results of e.m.f. measurements in hydrochloric acid solutions of different molalities (m) in the two solvent mixtures are given in Table 1, together with values of the total vapour pressures (v.p.) and dielectric constants of the two solvent mixtures

[1] Feakins and French, *J.*, 1956, 3168.
[2] *Idem*, *Chem. and Ind.*, 1954, 1107.
[3] Williams, Knight, and Crockford, *J. Amer. Chem. Soc.*, 1950, **72**, 1277.
[4] Lucasse, *Z. phys. Chem.*, 1926, **121**, 254.
[5] Harned and Nestler, *J. Amer. Chem. Soc.*, 1946, **68**, 665.
[6] Knight, Crockford, and James, *J. Phys. Chem.*, 1953, **57**, 463.
[7] Crockford and Schnoosky, *J. Amer. Chem. Soc.*, 1951, **73**, 4177.
[8] Müller, Raschka, and Wittmann, *Monatsh.*, 1927, **48**, 659.
[9] Claussen and French, *Trans. Faraday Soc.*, 1955, **51**, 708.
[10] Hills and Ives, *J.*, 1951, 305.
[11] Gallagher and Hibbert, *J. Amer. Chem. Soc.*, 1936, **58**, 813.
[12] Matignon, Moreau, and Dode, *Bull. Soc. chim. France*, 1934, **1**, 311.

If E_m° is the standard potential of the cell on the molal scale, then

$$E = E_m^\circ - 2\,(RT/F)\ln m\gamma_\pm$$

where $\gamma_\pm$ is the mean molal activity coefficient and E is the observed e.m.f. corrected to 760 mm. pressure.

Following the procedure outlined earlier,[1] we can obtain a quantity E_0' which is related to standard potential by the equation

$$E_m^\circ = E_0' + 2kB'm$$

As before, the plot of E_0' against molality should yield a straight line of negative slope $-2kB'$, from which the salting-out constant B' can be determined. Extrapolation to zero molality will give E_m°.

TABLE 1.

Molality (m)	E.m.f. (E) (v)	Molality (m)	E.m.f. (E) (v)	Molality (m)	E.m.f. (E) (v)	Molality (m)	E.m.f. (E) (v)
10% Methyl Ethyl Ketone: $\varepsilon = 71{\cdot}9$; V. p. = 69·4 ± 0·1 mm.; $E_m^\circ = 0{\cdot}2153_5$ v.				20% Methyl Ethyl Ketone: $\varepsilon = 74{\cdot}9$; V. p. = 93·9 ± 0·1 mm. $E_m^\circ = 0{\cdot}2078$ v.			
0·003455	$0{\cdot}5102_5$	0·01141	$0{\cdot}4512_5$	0·003125	$0{\cdot}5083_5$	0·01738	0·4242
0·004677	0·4951	0·02154	$0{\cdot}4203_5$	0·005136	0·4837	0·04000	0·3844
0·006591	0·4784	0·04586	0·3840	0·006423	0·4726	0·05940	$0{\cdot}3656_5$
0·006886	$0{\cdot}4760_5$	0·06705	$0{\cdot}3658_5$	0·008077	0·4614	0·08020	$0{\cdot}3514_5$
0·007307	$0{\cdot}4731_5$	0·08710	0·3535	0·01023	0·4499	0·1054	$0{\cdot}3386_5$
0·008361	0·4665	0·1139	$0{\cdot}3406_5$				
0·009869	$0{\cdot}4583_5$						

A value of 4·3 Å being used for the ionic parameter $\hat{a}$, straight lines (plotted by the method of least squares) were obtained over the concentration range 0·003—0·1m in both cases. The standard potentials and values of B' were obtained from these lines. Only in a few cases are the deviations of individual points from the straight lines as great as 0·2 mv. The standard potentials are probably accurate to at least ±0·1 mv.

Activity coefficients in the range 0·003—0·1m are obtained from the equation

$$\log_{10}\gamma_\pm = -Ac^{\frac{1}{2}}/(1 + \hat{a}Bc^{\frac{1}{2}}) + B'm - \log_{10}(1 + 0{\cdot}002M_{xy}m) \quad . \quad (1)$$

by employing the appropriate experimental values of B'. $M_{xy} = 100/[X/M_x + (100 - X)/M_y]$ where X is the weight percentage of the ketone, and M_x and M_y are the molecular weights of the ketone and water respectively.

The values of A, B, and B', the densities of the pure solvent mixtures (d_0) and the activity coefficients at rounded acid concentrations calculated from eqn. (1) are given in Table 2.

TABLE 2.

Methyl ethyl ketone (%)	10	20	m =	$\gamma_\pm$ =	0	10	20
A	0·5779	0·6740	0·002m		0·9521	0·947	0·939
B	0·3436	0·3617	0·005m		0·9285	0·920	0·908
B'	$0{\cdot}14_4$	$0{\cdot}15_1$	0·01m		0·9048	0·894	0·878
d_0	0·9844	0·9703	0·02m		0·8755	0·862	0·842
M_{xy}	19·46	21·18	0·05m		0·8304	0·813	0·787
			0·1m		0·7964	0·774	0·744

The standard potentials will be discussed in detail in the following paper, but there are a few points which may be noted. The plot of E_m° against $1/\varepsilon$ gives a curve which is closely related to one on which the results for propanol solutions and for 5% and 10% acetone solutions lie. As is usually the case when comparing solutions of homologous series, the E_m° values for ethyl methyl ketone solutions are higher, for isodielectric mixtures, than those for acetone solutions. This is also true for the E_N° against $1/\varepsilon$, and $E_N^\circ - k\log N_w$ against $1/\varepsilon$ plots. Here the ethyl methyl ketone curve shows a closer relation to the curve for the monohydric alcohols than it does to that for acetone. These considerations indicate that little further progress can be made with plots of this sort.

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On the other hand, the E_m° values of 10% and 20% solutions respectively of the two ketones differ only slightly. The generally close similarity between the solutions (both show strong positive deviations from Raoult's law, and the vapour pressures of the two 10% solutions are identical) is also interesting. Both these facts support the contention that the stoicheiometry of the solvent mixture, and to some extent its thermodynamic properties, are the major factors in determining E_m°. Up to concentrations of 20% (w/w) solutions of both ketones obey fairly closely the same simple stoicheiometric relation.

Appendix

Considerable and unexpected experimental difficulty was experienced in the measurement of e.m.f. in aqueous triethylene glycol solutions. This arose principally from the behaviour of the silver–silver chloride electrodes. These were prepared as described earlier,[9] but even when carefully washed between runs became, after the second or third time of use, 0·2—0·3 mv negative to a freshly prepared electrode. After a few more runs the electrodes exhibited deviations often amounting to 2 mv or more. This effect was particularly marked in the more concentrated acid solutions of the 20% glycol–water mixtures. At least one freshly prepared electrode was therefore used for each run, and no electrode was used more than 3 times.

The behaviour of the hydrogen electrodes was fairly satisfactory in these solutions. "Activated" electrodes (*i.e.*, the unplatinised electrodes described earlier [1,2]) were not uniformly successful, some showing a tendency to failure. Agreement between platinum-black electrodes was also often poor, and the best electrodes for these systems were very thinly plated grey ones, obtained by platinising from solutions containing no lead.[10]

Even with these precautions, cell agreement was often poor (three cells differing from the mean by more than 0·05 mv), and led to the rejection of many unsatisfactory runs. It was believed however, that the electrode behaviour, and the anomalous results discussed below, could not be ascribed to solvent impurity since most of the e.m.f. measurements were reproducible between different batches of glycol, as also were the physical constants.

Measurements in both the 10% and 20% solvent mixtures were made over the acid concentration range 0·003—0·1m. The 10% solution was studied in greater detail than the 20% solution, where repeated lack of agreement between the three cells would have necessitated a very large number of trials.

The results are shown in Table 3 where, in addition to the observed e.m.f. at each concentration, are given the appropriate values of E_0', computed on the basis of an $\mathring{a}$ value of 4·3 Å.

Table 3.

Molality (10^3m)	E(v)	E_0'	Molality (10^3m)	E(v)	E_0'	Molality (10^3m)	E(v)	E_0'
10% Triethylene glycol: $\varepsilon = 73{\cdot}0$; V. p. = 23·4 (± 0·1) mm; $E_m^\circ = 0{\cdot}2161_5$ v.								
3·175	$0{\cdot}5160_5$	0·2170	7·864	$0{\cdot}4707_5$	0·2165	51·27	$0{\cdot}3790_5$	0·2149
4·016	$0{\cdot}5044_5$	$0{\cdot}2170_5$	9·182	$0{\cdot}4628_5$	0·2162	53·12	0·3774	0·2152
5·174	$0{\cdot}4917_5$	0·2169	10·28	0·4573	$0{\cdot}2161_5$	61·30	0·3707	$0{\cdot}2149_5$
5·410	0·4895	0·2169	13·48	$0{\cdot}4441_5$	0·2162	69·59	$0{\cdot}3645_5$	0·2147
6·074	$0{\cdot}4838_5$	0·2169	18·01	$0{\cdot}4296_5$	0·2157	80·43	$0{\cdot}3574_5$	$0{\cdot}2143_5$
6·203	0·4829	0·2170	33·17	0·4001	0·2154	91·09	$0{\cdot}3515_5$	$0{\cdot}2142_5$
6·789	$0{\cdot}4779_5$	0·2165	39·95	0·3911	0·2152	98·43	0·3478	$0{\cdot}2140_5$
20% Triethylene glycol: $\varepsilon = 67{\cdot}0$; V. p. = 22·8 ± 0·1 mm.; $E_m^\circ = 0{\cdot}2094$ v.								
3·515	0·5059	0·2114	6·116	$0{\cdot}4779_5$	0·2107	39·22	$0{\cdot}3867_5$	$0{\cdot}2086_5$
3·603	$0{\cdot}5045_5$	0·2113	7·126	$0{\cdot}4699_5$	$0{\cdot}2101_5$	64·11	0·3629	0·2076
5·246	$0{\cdot}4856_5$	$0{\cdot}2108_5$	8·322	$0{\cdot}4621_5$	$0{\cdot}2099_5$	84·25	$0{\cdot}3496_5$	$0{\cdot}2070_5$
5·419	0·4839	0·2108	10·69	$0{\cdot}4490_5$	0·2090	96·43	$0{\cdot}3433_5$	$0{\cdot}2068_5$
5·966	$0{\cdot}4791_5$	0·2107	17·82	$0{\cdot}4243_5$	0·2088			

The plots of E_0' against molality are highly anomalous. Neither plot is the single straight line which is usually found: neither plot can be made a straight line over the

whole concentration range by adjusting $\hat{a}$. In the 10% solution a straight line relationship holds from about 0·02 to 0·1m. From 0·003 to 0·02m, E_0' falls off very rapidly with molality, dropping about 1·3 mv compared with a normal drop of about 0·4 mv. While the values of E_0' are sensibly constant over a very short range in the most dilute solutions, any extrapolation to obtain E_m° in concentrations below 0·02m would be extremely unreliable. Extrapolation of the results in the higher concentrations yields an E_m° value of $0{\cdot}2161_5$ v, and a salting-out constant B' of $0{\cdot}18_2$.

In the 20% solution there is again a very rapid drop in E_0' with increase in acid concentration in the region 0·003—0·01m. At higher concentrations the results lie on a straight line, which, on extrapolation to zero molality, yields an E_m° value of 0·2094 v, but with rather less certainty than in the 10% mixture. The salting-out constant B' is $0{\cdot}22_8$.

The uncertainty with which these values are obtained, owing to the lack of reliable measurements in the very dilute solutions, prevents our calculating activity coefficients. Further, although the trends in the dilute solutions are systematic, they are probably of experimental origin.

The B' values for triethylene glycol solutions are high compared with those found for solutions of simpler substances (0·13—0·17). Such high values are found also with glycerol, glucose, and fructose solutions if an $\hat{a}$ value of 4·3 is employed.

Finally it is interesting that the E_m° values for the 10% and 20% solutions agree well with those predicted by the stoicheiometric relation discussed in detail in the following paper ($0{\cdot}2162$ and $0{\cdot}2095_5$ respectively). Considered on the basis of isodielectric mixtures, the E_m° values, unlike those of glucose and to some extent glycerol solutions, are not anomalously low. Triethylene glycol solutions, and glycerol solutions generally, obey the stoicheiometric relationship fairly closely, whilst glucose solutions do not. Special reasons for the deviations in the latter systems are given in the following paper.

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440. *Carbonyl Complexes of Rhodium. Part I. Complexes with Triarylphosphines, Triarylarsines, and Triarylstibines.*

By (Miss) L. Vallarino.

The preparation and properties of a new series of complexes of rhodium(I) of general formula $[RhL_2(CO)X]$ (L = Ar_3P, Ar_3As, Ar_3Sb; X = Cl, I, SCN) are described. These compounds are monomeric, non-electrolytes in nitrobenzene, and diamagnetic. They are characterised by a remarkable stability, *e.g.*, the carbonyl group is not affected by cold alkali.

These complexes should be square planar, and measurements of dielectric constant in benzene seem to indicate that they have the *trans*-configuration.

It has recently been shown [1,2] that rhodium(I) forms very stable co-ordination compounds which, like those of palladium(II) and platinum(II), are four co-ordinate.

In view of the strong affinity of palladium(II) and platinum(II) for tertiary phosphines and the capacity of these ligands to stabilise low oxidation states of the central metal atom [3,4] it could be foreseen that rhodium(I), which is isoelectronic with palladium(II), would form stable complexes with tertiary phosphines.

[1] Malatesta and Vallarino, *J.*, 1956, 1867.
[2] Chatt and Venanzi, *Nature*, 1956, **177**, 852.
[3] Malatesta and Angoletta, *Atti Accad. naz. Lincei, Rend. Classe Sci. Fis. mat. nat.*, 1955, VIII, **19**, 43.
[4] *Idem, J.*, 1957, 1186.

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An ethanolic solution of hydrated rhodium trichloride, on treatment with an excess of an *iso*cyanide [1] or a chelating diolefin,[2] gives, directly, derivatives of rhodium(I), $[Rh(RNC)_4]Cl$ and $[Rh_2(diolefin)_2Cl_2]$, but reduction of a rhodium(III) salt in the presence of a derivative of arsenic(III) gives products which were though to be complexes of rhodium(II).[5] It has recently been found [6] that some of these compounds are diamagnetic, and Nyholm formulates them as mixed salts of rhodium(I) and rhodium(III).

For the preparation of the complexes of rhodium(I) with Group VB donors we used as a starting material tetracarbonyl-$\mu\mu'$-dichlorodirhodium, $[Rh_2(CO)_4Cl_2]$, because it already contains the metal in a +1 oxidation state, and it is the most easily prepared of the carbonyl halides of rhodium.[7]

A cold benzene solution of rhodium carbonyl chloride reacts very readily with triphenylphosphine, both as the solid and in benzene solution. A lively evolution of carbon monoxide occurs and from the solution, on evaporation of most of the solvent at 14 mm. and dilution of the concentrated solution with ethanol or hexane, a yellow crystalline product is obtained which is diamagnetic, does not conduct electricity in nitrobenzene solution, and on the basis of analysis and molecular-weight determination must be formulated as $[Rh(Ph_3P)_2(CO)Cl]$.

Rhodium carbonyl chloride reacts also with other triarylphosphines, and with triarylarsines and triarylstibines, to give products analogous to that obtained with triphenylphosphine. This reaction appears to be fairly general and can be written as:

$$[Rh_2(CO)_4Cl_2] + 4L \longrightarrow 2[RhL_2(CO)Cl] + 2CO \quad (L = Ar_3P, Ar_3As, \text{ or } Ar_3Sb)$$

The compounds characterised are listed in Table 1. Their thermal stability is considerable: they melt, with decomposition, in the range 150—250°. It is interesting that the arsine-containing complexes have decomposition points which, on average, are about 50° higher than those of the corresponding phosphorus compounds. The general stability of the stibine-containing complexes of rhodium(I) is comparable to that of analogous palladium(II) and platinum(II) derivatives.[8]

TABLE 1. *New complexes of the type* $[RhL_2(CO)Cl]$.

L	Decomp. pt.		L	Decomp. pt.	
Ph_3P	195—200°	Yellow prisms	$(p\text{-}C_6H_4Cl)_3As$	230—245°	Yellow prisms
$(p\text{-}C_6H_4Me)_3P$ ...	190—195	Deep yellow prisms	Ph_3Sb	151—153	Purple-red prisms
$(p\text{-}MeO\cdot C_6H_4)_3P$...	193—195	Yellow prisms	$(p\text{-}C_6H_4Me)_3Sb$	156—158	Red needles
$(p\text{-}C_6H_4Cl)_3P$	190—195	Yellow needles	$(p\text{-}C_6H_4Cl)_3Sb$...	160—162	Orange-red plates
Ph_3As	242—245	Yellow prisms	Ph_3P [a]	190—195	Yellow plates
$(p\text{-}C_6H_4Me)_3As$ ...	235—242	Deep yellow prisms	Ph_3P [b]	188—194	Yellow prisms
$(p\text{-}MeO\cdot C_6H_4)_3As$	235—240	Yellow prisms			

[a] Iodide. [b] Thiocyanate.

Another notable feature of the complexes $[RhL_2(CO)Cl]$ is their chemical inertness. They are not attacked by boiling dilute solutions of acids and bases, boiling concentrated hydrochloric acid, or cold alcoholic alkali hydroxides. The last, when hot, decompose the complexes with formation of amorphous brown products. These rhodium(I) derivatives do not tend to oxidise spontaneously and do not reduce silver nitrate or mercuric chloride. Their aqueous-alcoholic suspensions are not reduced by hypophosphorous acid, nor are their alcoholic suspensions by metallic magnesium or hydrazine hydrate. The chlorine atom in these compounds is fairly strongly bound. A benzene solution of silver perchlorate in the cold becomes cloudy only after several minutes. This chlorine atom is not replaced by bromine or iodine when an acetone solution is boiled with lithium bromide or iodide, but it is replaced by prolonged boiling of an acetone solution with an excess of sodium iodide or

[5] Dwyer and Nyholm, *J. Proc. Roy. Soc., New South Wales*, 1942, **75**, 122.
[6] See Nyholm, Proc. Solvay Conference, Brussels, 1956.
[7] Hieber and Lagally, *Z. anorg. Chem.*, 1943, **251**, 98.
[8] Chatt and Wilkins, *J.*, 1953, 70.

thiocyanate, probably because in this case the reaction is favoured by precipitation of sodium chloride. By this method the compounds $[Rh(Ph_3P)_2(CO)I]$ and $[Rh(Ph_3P)_2(CO)(SCN)]$ were obtained. The iodo-complex is less stable than its chloro-analogue, especially in solution, where it becomes brown within a few hours.

The difficulty encountered in replacing the chlorine atom by iodine is rather surprising. Rhodium(I) has its *d*-orbitals immediately under the valency shell filled, and gives strongly covalent complexes, very similar to those of palladium(II) and platinum(II) and therefore one would have expected the chlorine atoms to be quickly replaced by bromine and iodine, as happens with the complexes of palladium(II) and platinum(II).

The most striking feature of the complexes of type $[RhL_2(CO)Cl]$ is the stability of the carbon monoxide–metal bond. The complexes can be recovered in almost quantitative yield after 2 hours' boiling in xylene with an excess of ligand, L, or after boiling of a chloroform solution with an excess of pyridine or *p*-toluidine. The direct replacement of carbon monoxide from these complexes does not appear possible. The displacement of carbon monoxide by another ligand, when it occurs, is always accompanied by a complete change in the nature of the complex. This displacement occurs with triarylphosphites and aryl *iso*cyanides, thus:

$$[Rh(Ar_3P)_2(CO)Cl] + 3(ArO)_3P \longrightarrow [Rh\{(ArO)_3P\}_2Cl] + CO + 2Ar_3P$$

$$[Rh(Ar_3P)_2(CO)Cl] + 4ArNC \longrightarrow [Rh(ArNC)_4]Cl + CO + 2Ar_3P$$

The second reaction occurs particularly easily and can be carried out very quickly and quantitatively by mixing in the cold the solid complex with an excess of liquid *iso*cyanide, which also acts as a solvent. It has been used for the volumetric determination of carbon monoxide in the above compounds.

In analogy to the tetraco-ordinated complexes of palladium(II) and platinum(II), the compounds $[RhL_2(CO)Cl]$ should have square planar configuration and the rhodium atom dsp^2 hybridisation. On this basis our complexes should, at least in principle, be capable of existing in a *trans*-form (I) and a *cis*-form (II). In each case, however, only one form could be obtained and this does not appear to change on repeated recrystallisation from different solvents.

In an attempt to establish the geometrical configuration of the products which were isolated, the dielectric constant of a benzene solution of several of these compounds was measured at 25° and from this an approximate dipole moment was calculated by Jensen's approximate formula.[9] The values obtained for these moments are listed in Table 2.

TABLE 2. *Approximate dipole moments* (μ, D) *of the complexes* $[Rh\{(p\text{-}X\cdot C_6H_4)_3M\}_2(CO)Cl]$.

	X	H	Me	Cl	OMe
M = P	.....	3·15	3·1	2·5	4·0
M = As	.....	3·2	3·6	2·9	Unknown

The dipole moments are all rather low for co-ordination compounds and consequently little value can be attributed to the absolute figures obtained, in view of the uncertainties about the contributions of the electron and atom polarisation. The relative moments of the bonds Rh–PR_3, Rh–AsR_3, Rh–CO, and Rh–Cl are not known, but one can, as a first approximation, assume that they do not differ appreciably from those of the corresponding bonds to platinum(II). The complex *cis*-$[Pt(CO)_2Cl_2]$ has $\mu = 4{\cdot}65$ D,[10] and the *cis*-$[Pt(R_3M)_2Cl_2]$ (M = P, As, or Sb) have $\mu = 10$—11 D.[11] From these figures one would

[9] Jensen, *Z. anorg. Chem.*, 1936, **229**, 250.
[10] Chatt and Williams, *J.*, 1951, 3061.
[11] Chatt and Wilkins, *J.*, 1952, 4300.

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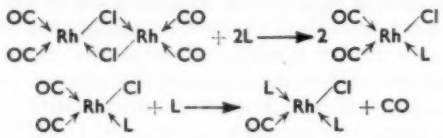
expect dipole moments of the order of 3—3·5 D for the *trans*-isomer (I), and 8—9 D for the *cis*-isomer (II). The values given in Table 2 come within the range of a *trans*-isomer.

This conclusion is also supported by the possible reaction mechanism based on the assumption that the *trans*-effect [12] is operative in complexes of rhodium(I):



The lower stability of the iodo-complex $[Rh(Ph_3P)_2(CO)I]$ is also in agreement with this configurational assignment and the relative position of these two halide ions in the *trans*-effect scale.

On the other hand, changing the substituent X on the benzene ring, in *para*-position to the donor atom M, should not appreciably change the dipole moment if the complex has *trans*-configuration. The differences observed are too small to be caused by a *cis*-configuration in the complex. These results could be explained by assuming that in benzene solution an equilibrium is established between the two isomers, consisting mainly of the *trans*-form, but containing small amounts of *cis*-form which vary with the nature of the donor atom M and the *para*-group X. The existence of such equilibria in benzene solution for complexes of the type $[PtL_2Cl_2]$ and $[PdL_2Cl_2]$, where L = R_3P, R_3As, or R_3Sb,[8,11] is well known, and in these cases the equilibrium position varies with the nature of R.

Experimental

Tetracarbonyl-μμ′-dichlorodirhodium(I) $[Rh_2(CO)_4Cl_2]$.—This was prepared by Hieber and Lagally's method [7] and purified by extracting the mixture with boiling hexane, filtering the hot solution, and cooling it to −20°. The product separated in long orange-red needles (Found: CO, 29·3; Rh, 53·0. Calc. for $C_4O_4Cl_2Rh_2$: CO, 28·8; Rh, 52·9%).

Carbonylbis(triphenylphosphine)chlororhodium(I) $[Rh(Ph_3P)_2(CO)Cl]$.—Triphenylphosphine (0·90 g., 3·5 mmols.) was added to a solution of tetracarbonyldichlorodirhodium(I) (0·225 g., 0·58 mmols.) in benzene (60 ml.). A lively reaction occurred with evolution of carbon monoxide (palladous chloride test). The solution was evaporated to a small volume at 15 mm. and then diluted with ethanol (40 ml.). A yellow crystalline product gradually separated; it was filtered off, washed with ether, and dried (1·05 g.). Recrystallisation was effected by dissolving the crude product in chloroform and diluting the solution with ethanol (yield 0·80 g.) (Found: CO, 3·9; Cl, 5·1; P, 9·1; Rh, 15·1%; *M*, cryoscopic in 2·5% nitrobenzene solution, 740. $C_{37}H_{30}OClP_2Rh$ requires CO, 4·05; Cl, 5·1; P, 9·0; Rh, 14·9%; *M*, 691). $\chi_M = -513 \times 10^{-6}$. The *complex* is very soluble in methylene chloride and chloroform, soluble in carbon tetrachloride, benzene and its homologues, and nitrobenzene, slightly soluble in acetone and ethyl ether, and insoluble in methanol, ethanol, and hexane.

This compound is also obtained by using the stoicheiometric amount of triphenylphosphine or a larger excess.

Attempted reaction with an excess of triphenylphosphine. The complex (0·3 g.) and triphenylphosphine (0·5 g.) in xylene (15 ml.) were refluxed for 2 hr. After cooling, methanol (40 ml.) was added. Crystals slowly separated, and were filtered off, washed with ether, and purified as described for the starting material (yield 0·25 g.). They constituted starting material, as shown by the infrared spectrum.

Attempted reaction with lithium bromide and lithium iodide. The complex (0·6 g.) in acetone (50 ml.) was boiled for 15 min. with lithium bromide (0·1 g.). There was no apparent colour change. The solution was evaporated to a small volume at 15 mm. pressure and diluted with methanol. The starting material was thus recovered (0·4 g.) and identified by its infrared spectrum.

When this reaction was carried out with lithium iodide instead of lithium bromide, a brown

[12] Chatt, Duncanson, and Venanzi, *J.*, 1955, 4456, and references quoted therein.

solution was obtained, but on dilution with methanol the unchanged starting material was recovered (0·3 g.) and identified by its infrared spectrum.

Attempted reaction with p-*toluidine and pyridine.* The complex (0·15 g.) in chloroform (10 ml.) was refluxed for 30 min. with *p*-toluidine (0·15 g.). On dilution with methanol crystals separated (0·12 g.); these did not contain nitrogen and the infrared spectrum was identical with that of the starting material.

Using pyridine (0·5 ml.) instead of *p*-toluidine, under the same conditions, gave starting material (0·1 g.), identified by its infrared spectrum.

*Reaction with tri-*p-*chlorophenyl phosphite.* The complex (0·2 g.) in chloroform (10 ml.) and tri-*p*-chlorophenyl phosphite (0·1 g.) were boiled for a few minutes. The solution was taken to dryness at 15 mm. and the residual yellow oil was washed with hexane, then dissolved in benzene, and the solution diluted with hexane. Crystals (0·11 g.) were obtained which, from the infrared spectrum, were starting material.

This reaction, with 2 mols. of tri-*p*-chlorophenyl phosphite per mole of complex, gave a mixture of yellow crystalline products (as shown under a microscope), still containing carbon monoxide, which was evolved on addition of aryl *iso*cyanides.

Using 3 mols. of tri-*p*-chlorophenyl phosphite per mole of complex under the above conditions, gave *tris*-(p-*chlorophenyl phosphite*)*chlororhodium*, $[Rh\{(p\text{-}Cl\cdot C_6H_4\cdot O)_3P\}_3Cl]$ (0·7 g. from 0·6 g.) (Found: P, 6·9; Rh, 7·6. $C_{54}H_{36}O_9Cl_{10}P_3Rh$ requires P, 6·7; Rh, 7·5%). Its infrared spectrum is identical with that of the product obtained by direct reaction of tri-*p*-chlorophenyl phosphite and rhodium carbonyl chloride which will be described later.

Reaction with p-*tolyl* iso*cyanide.* *p*-Tolyl *iso*cyanide (1 mmole) was added to the solid complex (0·1 mmole); a gas was evolved immediately and the reaction was taken to completion by warming the mixture to 50—60° for 2 min. The gas evolved was measured in a Lunge's burette filled with mercury (Found: 2·18 ml., 0·0965 mmol.), and identified as pure carbon monoxide (palladous chloride test and ammoniacal cuprous chloride).

The reaction mixture was dissolved in ethanol (40 ml.) and filtered after treatment with charcoal. On addition of sodium perchlorate in ethanol violet crystals separated which, in boiling benzene, gave yellow plates of *tetra*-p-*tolyl*iso*cyanorhodium*(I) *perchlorate* (Found: N, 8·5; Rh, 15·5. $C_{32}H_{28}O_4N_4ClRh$ requires N, 8·3; Rh, 15·35%).

Carbonylbis(*triphenylphosphine*)*iodorhodium*(I) $[Rh(Ph_3P)_2(CO)I]$.—The corresponding chloride (0·4 g.) and sodium iodide (0·2 g.) in acetone (20 ml.) were refluxed for 30 min. The solution was taken to dryness at 15 mm. The solid residue was extracted with benzene, and the solution filtered. Diluting this solution with hexane gave crystals slowly (0·3 g.). The new *complex* was purified by dissolving it in hot benzene and reprecipitating it with hexane (Found: C, 56·5; H, 3·8; I, 16·3. $C_{37}H_{30}OIP_2Rh$ requires C, 56·8; H, 3·9; I, 16·2%). It is diamagnetic, and less soluble than its chloro-analogue. It is stable in the crystalline state but its solutions darken within a few hours.

Carbonylbis(*triphenylphosphine*)*thiocyanatorhodium*(I) $[Rh(Ph_3P)_2(CO)(SCN)]$.—This *compound* was prepared analogously to the iodide, from the corresponding chloride (0·6 g.) and sodium thiocyanate (0·3 g.) in acetone (50 ml.), and purified as its chloro-analogue (yield 0·45 g.). It is diamagnetic (Found: N, 2·15; S, 4·7; CO, 3·7%; *M*, cryoscopic in 2·2% bromoform solution, 730. $C_{38}H_{30}ONSP_2Rh$ requires N, 2·0; S, 4·5; CO, 3·9%; *M*, 713). It appears to be much less soluble than its chloro-analogue.

The following compounds were prepared and purified analogously to the carbonylbis(triphenylphosphine)chlororhodium:

Carbonylbis(*tri-*p-*tolylphosphine*)*chlororhodium*(I) $[Rh\{(p\text{-}C_6H_4Me)_3P\}_2(CO)Cl]$ (Found: Cl, 4·75; P, 7·95; Rh, 13·6; CO, 3·7%; *M*, cryoscopic in 3·0% nitrobenzene solution, 722. $C_{43}H_{42}OClP_2Rh$ requires Cl, 4·6; P, 8·0; Rh, 13·3; CO, 3·6%; *M*, 775). $\chi_M = -480 \times 10^{-6}$.

Carbonylbis(*tri-*p-*methoxyphenylphosphine*)*chlororhodium*(I) $[Rh\{(p\text{-}MeO\cdot C_6H_4)_3P\}_2(CO)Cl]$ (Found: Cl, 4·05; P, 7·1; Rh, 11·7%; *M*, cryoscopic in 1·1% benzene solution, 822. $C_{43}H_{42}O_7ClP_2Rh$ requires Cl, 4·1; P, 7·1; Rh, 11·8%; *M*, 871). $\chi_M = -574 \times 10^{-6}$.

Carbonylbis(*tri-*p-*chlorophenylphosphine*)*chlororhodium*(I) $[Rh\{(p\text{-}C_6H_4Cl)_3P\}_2(CO)Cl]$ (Found: Cl, 27·9; P, 7·1; Rh, 11·65%; *M*, cryoscopic in 1·4% benzene solution, 813. $C_{37}H_{24}OCl_7P_2Rh$ requires Cl, 27·65; P, 6·9; Rh, 11·5%; *M*, 898). $\chi_M = -426 \times 10^{-6}$.

Carbonylbis(*triphenylarsine*)*chlororhodium*(I) $[Rh(Ph_3As)_2(CO)Cl]$ (Found: Cl, 4·7; As, 19·0; Rh, 13·2; CO, 3·4%; *M*, cryoscopic in 1·3% benzene solution, 769. $C_{37}H_{30}OClAs_2Rh$ requires Cl, 4·55; As, 19·2; Rh, 13·2; CO, 3·6%; *M*, 779). $\chi_M = -325 \times 10^{-6}$.

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Carbonylbis(tri-p-tolylarsine)chlororhodium(I) $[Rh\{(p\text{-}C_6H_4Me)_3As\}_2(CO)Cl]$ (Found: Cl, 4·2; As, 17·4; Rh, 12·0%; *M*, cryoscopic in 1·6% benzene solution, 835. $C_{43}H_{42}OClAs_2Rh$ requires Cl, 4·1; As, 17·4; Rh, 11·9%; *M*, 863). $\chi_M = -488 \times 10^{-6}$.

Carbonylbis(tri-p-methoxyphenylarsine)chlororhodium(I) $[Rh\{(p\text{-}MeO\text{-}C_6H_4)_3As\}_2(CO)Cl]$ (Found: Cl, 3·7; As, 15·75; Rh, 10·9%; *M*, cryoscopic in 1·1% nitrobenzene solution, 928. $C_{43}H_{42}O_7ClAs_2Rh$ requires Cl, 3·7; As, 15·6; Rh, 10·7%; *M*, 959). $\chi_M = -552 \times 10^{-6}$.

Carbonylbis(tri-p-chlorophenylarsine)chlororhodium(I) $[Rh\{(p\text{-}C_6H_4Cl)_3As\}_2(CO)Cl]$ (Found: Cl, 25·8; As, 15·3; Rh, 10·4%; *M*, cryoscopic in 1·0% benzene solution, 968. $C_{37}H_{24}OCl_7As_2Rh$ requires Cl, 25·2; As, 15·2; Rh, 10·4%. *M*, 986). $\chi_M = -394 \times 10^{-6}$.

Reaction of Carbonylbis(triphenylarsine)chlororhodium with Tri-p-chlorophenyl Phosphite.—The reaction was carried out as described for the triphenylphosphine derivative. (1) With 1 or 2 mols. of tri-*p*-chlorophenyl phosphite a mixture of crystalline products was obtained, which evolved carbon monoxide with aryl *iso*cyanides. (2) With 3 mols. of phosphite tris(tri-*p*-chlorophenyl phosphite)chlororhodium was obtained, as shown by its infrared spectrum.

Carbonylbis(triphenylstibine)chlororhodium(I) $[Rh(Ph_3Sb)_2(CO)Cl]$.—This *complex* was prepared analogously to the triphenylphosphine derivative and purified by dissolving the crude product in methylene chloride and reprecipitating it with di*iso*propyl ether (Found: Cl, 4·1; Sb, 28·0; Rh, 11·55%; *M*, cryoscopic in 0·98% benzene solution, 795. $C_{37}H_{30}OClSb_2Rh$ requires Cl, 4·1; Sb, 27·9; Rh, 11·8%; *M*, 872·5). $\chi_M = -248 \times 10^{-6}$. It is more soluble than the corresponding phosphine and arsine derivatives.

The following were prepared and purified as described for their phenyl analogue:

Carbonylbis(tri-p-tolylstibine)chlororhodium(I) (Found: Cl, 3·65; Sb, 26·0; Rh, 10·5%; *M*, cryoscopic in 2·1% benzene solution, 965. $C_{43}H_{42}OClSb_2Rh$ requires Cl, 3·7; Sb, 25·45; Rh, 10·8%; *M*, 957). $\chi_M = -605 \times 10^{-6}$.

Carbonylbis(tri-p-chlorophenylstibine)chlororhodium(I) (Found: Cl, 22·7; Sb, 22·7; Rh, 9·3%; *M*, cryoscopic in 1·6% benzene solution, 968. $C_{37}H_{24}OCl_7Sb_2Rh$ requires Cl, 23·0; Sb, 22·6; Rh, 9·5%; *M*, 1079). $\chi_M = -342 \times 10^{-6}$.

Reaction of Carbonylbis(triphenylstibine)chlororhodium(I) *with Tri-p-chlorophenyl Phosphite.*—This reaction was carried out as for the corresponding phosphine derivative. (1) With 1 or 2 mols. of phosphite a mixture of yellow and orange products was obtained. From this repeated recrystallisation gave pure tris(tri-*p*-chlorophenyl phosphite)chlororhodium. (2) With 3 mols. of phosphite, tris(tri-*p*-chlorophenyl phosphite)chlororhodium was obtained in good yield. These products were identified by their infrared spectra.

Conductivity Measurements.—None of the compounds described conducts electricity in a 10^{-3} molal nitrobenzene solution at 20°.

Magnetic Moments.—These were determined by a Gouy balance at 20°.

Dipole Moments.—The dielectric constants of benzene solutions of the tertiary phosphine and arsine derivatives were measured at 25° on an apparatus kindly made available by Dr. J. Chatt, Akers Research Laboratories, Imperial Chemical Industries Limited, The Frythe, Welwyn, Herts. From the values of the dielectric constants the dipole moments were calculated by Jensen's approximate formula.[9]

Infrared Spectra.—The compounds were finely ground and suspended in Vaseline. Their infrared spectra were determined with a Perkin-Elmer (type 21) spectrophotometer with a rock-salt prisms and cell. No compensation was made for the absorption of the Vaseline. The author is indebted to Istituto di Chimica Industriale del Politecnico-Milano, for these measurements.

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441. *The* a priori *Calculation of Molecular Relaxation Times from the Shapes and Other Known Properties of Molecules.*

By J. Y. H. Chau, R. J. W. Le Fèvre, and J. Tardif.

Measurements are recorded of the relaxation times of nitrobenzene, 1-nitronaphthalene, 4-nitrodiphenyl, 9-nitroanthracene, benzophenone, fluorenone, pyridine, quinoline, *iso*quinoline, and acridine in a variety of solvents chosen from dioxan, *p*-xylene, carbon tetrachloride, benzene, toluene, *cyclo*hexane, *n*-heptane, and *n*-hexane. Equations are developed empirically, and tested against data from experiments, whereby τ may be computed *a priori* from shape or polarisability ellipsoids of the solute molecules, and the viscosities, depolarisation factors, and dielectric constants of the solvents.

Debye's treatment [1] of dielectric loss led to the well-known equation (1) for the relaxation time τ of a molecule of radius r in a medium having a coefficient of inner friction η_1^*:

$$\tau = 4\pi\eta_1^* r^3/kT \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (1)$$

As often used, with the macroscopic viscosity η_1 in place of the inaccessible η_1^*, and r^3 deduced from the molecular volume, eqn. (1) yields values of τ which may be 5—10 times those indicated by experiment. Two possible reasons for this are the non-equality of η_1^* and η_1 and the unreality of taking a sphere as a general model of all molecules. The former point has often been illustrated [2] and attention was early drawn to the latter by Perrin,[3] who suggested essentially the substitution of r^3 by the product of the three semi-axes of an ellipsoid. Perrin's idea has been elaborated by Fischer, Wirtz, and their collaborators,[4] while improved approximations to η_1^* have been suggested by Hill [5] and Hase; [6] these proposals will be considered later. At the outset our objective was the modification of eqn. (1) to improve its applicability to the *a priori* computation of the relaxation times of solutes at infinite dilution. Some recent success with the use of shape factors in related fields [7] encouraged the belief that they could be profitably introduced here. Accordingly the plan has been to determine τ for a standard molecule (nitrobenzene), in eight solvents, to attempt to fit it with certain properties of the media, and then to test the validities of any expressions so achieved on a variety of other solutes, 1-nitronaphthalene, 9-nitroanthracene, 4-nitrodiphenyl; and pyridine, quinoline, acridine, and *iso*quinoline, chosen for their obvious stereochemical relationships with nitrobenzene and pyridine.

Our results for relaxation times of nitrobenzene (10^{-12} sec.) were as follows (that for carbon disulphide is due to Whiffen [8]): Dioxan 21, *p*-xylene 14, carbon tetrachloride 14, benzene 11, toluene 11, carbon disulphide 8·6, *cyclo*hexane 9·3, *n*-heptane 6·4, *n*-hexane 6·8. These values appear in reasonable agreement with others, as follows (references in parentheses): Benzene 11·3 (10), 11·6 (11), 11·5 (12), 13·0 (13), 13·2 (14), 12·8 (8), 14·9 (6); carbon tetrachloride 15·2 (8), 19·6 (6); *cyclo*hexane 9·5 (8), 11·8 (6); *n*-hexane 8·5 (6); *n*-heptane 6·8 (8). (It should be mentioned that the measurements by Fischer *et al.* and

[1] Debye, "Polar Molecules," Reinhold Publ. Corp., New York, 1929, Chap. V.
[2] *E.g.*, Various authors in "Dielectrics," *Trans. Faraday Soc.*, 1946, **42**, Appendix.
[3] Perrin, *J. Phys. Radium*, 1934, **5**, 497.
[4] (*a*) Budo, Fischer, and Miyamoto, *Physikal. Z.*, 1939, **40**, 337; (*b*) Fischer, *ibid.*, p. 645; (*c*) Fischer, *Z. Physik*, 1949, **127**, 49; (*d*) Spernol and Wirtz, *Z. Naturforsch.*, 1953, **8a**, 522; (*e*) Gierer and Wirtz, *ibid.*, p. 532.
[5] Hill, *Proc. Phys. Soc.*, 1954, **67**, *B*, 149.
[6] Hase, *Z. Naturforsch.*, 1953, **8a**, 695.
[7] Barclay and Le Fèvre, *J.*, 1950, 556; Holland and Le Fèvre, *ibid.*, p. 2166; Angyal, Barclay, and Le Fèvre, *ibid.*, p. 3370; Buckingham and Le Fèvre, *J.*, 1952, 1932; Le Fèvre, "Dipole Moments," Methuen, London 3rd edn., 1953, pp. 82, 83; Le Fèvre and Le Fèvre, *Rev. Pure Appl. Chem.*, 1955, **5**, 287.
[8] Whiffen, *Trans. Faraday Soc.*, 1950, **46**, 130.

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TABLE 1. *Some properties of the solvents used.**

	$10^2\eta$ (P)	ε_{20}	Δ	V_{20} (c.c.)	$10^{24}r^3$ (c.c.)	$10^{25}\alpha_1$ (mean)
Dioxan	1·41	2·218	0·14	85·1	25·2	94·4
p-Xylene	0·64	2·270	0·63—0·64	123	36·4	141·2
CCl_4	0·97	2·238	0·048—0·056	96·6	28·6	105
C_6H_6	0·65	2·284	0·42—0·43	88·7	26·3	103·2
C_6H_5·Me	0·59	2·379	0·43—0·47	106	31·4	122·4
CS_2	0·37	2·641	0·64—0·68	60·2	17·8	83·45
cyclo-C_6H_{12}	0·97	2·023	0·063	108	32·0	108·7
C_7H_{16}	0·41	1·924	0·106	146	43·3	136·1
C_6H_{14}	0·32	1·890	0·087	130	38·5	117·8

For definition of symbols, see text. Viscosities, refractive indexes, and densities at 25° are from Timmermans, " Physicochemical constants of pure organic compounds," Elsevier, Amsterdam, 1950. Dielectric constants also therefrom and Maryott and Smith, " Table of dielectric constants of pure liquids," Nat. Bur. Stand. Circular 514, 1951. Depolarisation factors from Stuart, " Die Struktur des Freien Moleküls," Springer, Berlin, 1952, p. 356. Mean polarisabilities, α, calc. from R_D; $r^3 = 0{\cdot}6667 \cdot 10^{-8}\ V^{1/3}$ cm.

TABLE 2. *Dimensions and polarisabilities of solutes.*

	10^8A	10^8B	10^8C	$10^{24}ABC/8$	$10^{25}\alpha_{mean}$
C_6H_5·NO_2	8·00	6·05	2·90	17·4	129
1-NO_2·$C_{10}H_7$	8·00	8·70	2·90	25·2	197
9-NO_2·$C_{14}H_9$	8·00	10·91	2·90	31·6	292
p-NO_2·C_6H_4·Ph	12·32	6·05	2·90	27·0 [a]	222
"	12·32	6·05	6·05	56·4 [b]	222
C_5H_5N	6·1	6·2	2·9	13·7	91·3
C_9H_7N	6·1	8·7	2·9	19·3	156
iso-C_9H_7N	7·7	7·3	2·9	20·4	163
$C_{13}H_9N$	6·1	11·1	2·9	24·5	227

Rings are taken as [a] coplanar, [b] orthogonal.

TABLE 3. *Relaxation times* (10^{-12} *sec.*) *for nitrobenzene in various solvents.*

	Calc. from eqn.					Calc. from eqn.			
	(1)	(2)	(3)	Obs.*		(1)	(2)	(3)	Obs.*
Dioxan	132	20	21	20—23	CS_2	35	8·0—8·4	8·2—8·6	8·6
p-Xylene	60	15	15—16	13—14	*cyclo*-C_6H_4	91	13	14	9—12
CCl_4	91	13	13	13—20	*n*-C_7H_{16}	38	6·1	6·3	6·4
C_6H_6	61	12	13	11—15	*n*-C_6H_{14}	30	4·6	4·9	6·8—8·5
PhMe	55	11	11—12	11					

* Covering data from p. 2293.

Hase differ from the remainder in being made calorimetrically[9] at a wavelength of 3·4 m.) Correlations were sought between the values of τ given and many separate solvent properties, *e.g.*, adiabatic or isothermal compressibilities, and others considered earlier by Le Fèvre,[15] besides those collected in Table 1, from which it is evident that the relaxation does not follow viscosity, volume functions such as V_1/V_2, $\exp(-V_1/V_2)$, $\eta\exp(-V_1/V_2)$ etc., or others involving in a similar manner the polarisability ratios α_1/α_2. (For nitrobenzene at 20°: $V = 102$ c.c., $r^3 = 30{\cdot}2 \times 10^{-24}$ c.c., and $\alpha_{mean} = 129 \times 10^{-25}$ c.c.) By inspection it appeared that the products of the viscosities of Table 1 and some measure of the anisotropies of the solvents concerned would be more smoothly related with τ than are the viscosities themselves. Eventually it was found that $(\eta\exp\Delta)/(\varepsilon + 2)$ could be plotted fairly linearly against τ; here Δ is the depolarisation factor observed in (Rayleigh) scattered light from the liquid, ε the dielectric constant, and η a viscosity of the order of magnitude of a centipoise. Since Le Fèvre and Sullivan [16] had already noted a rough

[9] Fischer and Frank, *Physikal. Z.*, 1939, **40**, 435.
[10] Henrion, quoted in ref. 7.
[11] Jackson and Powles, ref. 2, p. 101.
[12] Whiffen and Thompson, *ibid.*, p. 114.
[13] Cripwell and Sutherland, *ibid.*, p. 149.
[14] Fischer, *Z. Naturforsch.*, 1949, **4a**, 707.
[15] Le Fèvre, ref. 2, p. 162.
[16] Le Fèvre and Sullivan, *J.*, 1954, 2873.

correlation of τ with the mean polarisabilities and the shapes of solutes, the empirical equation (2) immediately followed:

$$\tau = 4\pi\eta_1\alpha_{mean}(\exp \Delta_1)(\exp h^2)^2/(\varepsilon_1 + 2)kT \quad . \quad . \quad . \quad . \quad . \quad (2)$$

(h is defined by Holland and Le Fèvre.[7])

It happens that $(\alpha_{mean})(\exp h^2)^2$ is often numerically close to $ABC/8$ (A, B, and C are defined in ref. 7), *e.g.*, for nitrobenzene the values are $17{\cdot}00 \times 10^{-24}$ and $17{\cdot}40 \times 10^{-24}$ respectively. Equation (3) accordingly became an alternative to (2):

$$\tau = \pi\eta_1(\exp \Delta_1)ABC/2(\varepsilon_1 + 2)kT \quad . \quad . \quad . \quad . \quad . \quad (3)$$

(In equations 1—3 the subscript 1 is used to distinguish solvent properties from those of the solute.) The applicability of equations (1), (2), and (3) to nitrobenzene as solute is shown as Table 3; the requisite quantities A, B, C, and α_{mean} are given in Table 2 together with data to be used later in this paper.

Predictions of τ based on equations (2) and (3) being in reasonable accord with values obtained by experiment, the work has been extended to cover seven other solutes (see Table 4).

TABLE 4. *Relaxation times* (10^{-12} *sec.*) *for other solutes in various solvents.*

Solvent	Calc. from eqn. (2)	Calc. from eqn. (3)	Obs.
α-Nitronaphthalene			
Dioxan	32	30	23
p-Xylene	23	22	21
CCl_4	20	19	25
C_6H_6	19	18	20
PhMe	17—18	16—17	21
cyclo-C_6H_{12}	21	20	16
n-C_7H_{16}	9·7	9·1	14
n-C_6H_{14}	7·3	7·0	13
9-*Nitroanthracene*			
p-Xylene	38—39	28	30
CCl_4	33	24	23
C_6H_6	32	23	28
n-C_7H_{14}	12	11	11
Pyridine			
CCl_4	8·2—8·3	10	7·2
C_6H_6	7·9—8·0	10	4·4
n-C_7H_{44}	3·9	4·9	2·2

Solvent	Calc. from eqn. (2)	Calc. from eqn. (3)	Obs.
Quinoline			
CCl_4	16	14—15	14
C_6H_6	15	14	10
n-C_7H_{14}	7·7	6·9	6·0
iso*Quinoline*			
CCl_4	15	15—16	21
C_6H_6	15	14—15	15
n-C_7H_{14}	7·3	7·3	7·2
Acridine			
CCl_4	28	18—19	26
C_6H_6	27	18	20

4-Nitrodiphenyl

	Calc. from eqn. (2) [a]	Calc. from eqn. (3) [b]	Calc. from eqn. (3) [a]	Obs.
Dioxan	49	67	32	25
p-Xylene	35	49—50	24	23
CCl_4	31	42—43	20	21
C_6H_6	29	40—41	19—20	30

Rings are taken as [a] coplanar, [b] orthogonal.

Previous Empirical Approaches to the Problem.—Fischer,[4] starting from Perrin's idea [3] and elaborating his own earlier suggestions,[4a,b] proposed the equation: $\tau = 4\pi\eta fabc/4{\cdot}3kT$ in which a, b, and c are half-axes obtained similarly to our A, B, and C and f is a shape factor, dependent upon b/a and c/a (values are tabulated by Budó, Fischer, and Miyamoto [4a]), relating the τ of an ellipsoidal model to the τ of a sphere of equal volume. Applicability to measurements in benzene seems fairly good—values observed, as quoted in ref. 14 (in parentheses), follow those calculated (10^{-12} sec.): Me_2CO, 3·6 (3·3); $CHCl_3$, 7·0 (8·4); PhBr, 13 (12); $PhNO_2$, 11 (13). However, as Davies [17] has noted, "this apparently satisfactory . . . representation of the results is lost when the solvent is varied."

[17] Davies, *Quart. Rev.*, 1954, **8**, 250.

More recently, instead of using a constant multiplier η_i (as was first done by Fischer [45]), the needed coefficient of inner friction has been treated as a quantity dependent on *both* solute and solvent. Hase [6] puts $\eta_{micro} = \eta_{macro}$(function of V_2^*/V_1^*), where $V_1^* = 4\pi P_i Q_i R_i/3$, with P_i, Q_i, and R_i having the origin and significance of $A/2$, $B/2$, and $C/2$ (Table 2); asterisks are used to differentiate the V's from those, derived from densities and molecular weights, listed in Table 1. Hase accordingly writes $\tau = (3\eta f V_2^*/kT) \exp(-\Delta V_1^*/V_2^*)$, and from extant data on τ in a number of media deduces that α is a property of the solute molecule. His Table 8 however shows that it may lie between 0·4 and 2·5, and as α is apparently not predictable his equation cannot be used to provide τ *a priori*.

Wirtz and collaborators [4d,e] derive a "micro-friction factor" f_r of rotation, given by $f_{rot.} = [(6r_1/r_2) + (1 + r_1/r_2)^{-3}]^{-1}$ in which the radii r_1 and r_2 are obtained as $(0{\cdot}556V_i/\pi N)^{1/3}$ (where $V_i = M_i/d_i$). The relaxation time therefore becomes $\tau = 4\pi\eta_i r_2^3 f_{rot.}/kT$. A test with nitrobenzene gives the following:

Solvent	(r_2/r_1) *	$\tau_{calc.}$	$\tau_{obs.}$	Solvent	(r_2/r_1) *	$\tau_{calc.}$	$\tau_{obs.}$
cyclo-C_6H_{12}	0·98	19	7·6—12	CS_2	1·19	8·9	8·6
C_6H_6	1·05	14	11—15	CCl_4	1·02	20	13—20

* From ref. 4*d*.

The agreement between $\tau_{obs.}$ and $\tau_{calc.}$ is slightly inferior to that displayed in Table 3, but r_2 cannot be evaluated for a dissolved solid. An analogous disability affects Hill's promising treatment [5] whereby $\tau =$ (function of moments of inertia and masses of the solvent and solute molecules) $\times$ ("mutual viscosity" of solvent and solute)$/2kT$. Unfortunately it appears necessary to know η_2 before the "mutual viscosity" can be computed.

Accordingly we claim that equations (2) and (3) have a wider usefulness than others suggested.

Experimental

Materials.—These were recrystallised or redistilled, as appropriate, and had the properties recorded for pure specimens; 9-nitroanthracene was obtained by direct nitration; [18] the heterocyclic bases were B.D.H. samples treated as set out in ref. 19.

Methods and Apparatus.—The equipment used was that of Le Fèvre and Sullivan [16] who gave dimensional details of the E_{010} cavity resonator involved, but deal only briefly with the general procedures of measurement. The following notes may therefore be useful.

The essential components (see Figure) are: (1) two 10 cm. oscillators, *A* and *B* built around CV-35 Klystrons, and containing voltage-regulated power supplies; in oscillator *A* two of the

Table 5. *Solvent constants additional to those listed by Le Fèvre and Sullivan.*[16]

$T°$ (K)	ε	d	D	$T°$ (K)	ε	d	D
	Dioxan				cyclo*Hexane*		
288	2·226	1·0392	8·337	288	2·031	0·7831	6·265
293	$2{\cdot}217_5$	1·0336	8·291	293	2·023	0·7785	6·228
	Toluene				n-*Hexane*		
288	2·403	0·8716	7·032	288	1·898	0·6639	5·315
293	2·391	0·8669	6·991	293	1·890	0·6594	5·279
	p-*Xylene*				n-*Heptane*		
288	2·278	0·8654	6·952	288	1·931	0·6878	5·504
293	2·270	0·8610	6·916	293	1·924	0·6837	5·472

three brass slugs attached to the cavity of the Klystron are kept fixed, the remaining slug being insertable by a slow-motion fine control graduated over an arbitrary linear scale (readings on which are referred to as "frequency vernier settings"); (2) the cavity resonator described in ref. 16; (3) a crystal rectifier *X*, and galvanometer *G*, plus lamp and scale; (4) a quarter-wave co-axial cavity mixer; (5) a calibrated intermediate-frequency receiver readable to 0·01 Mc./sec. between 13·5 and 18·5 Mc./sec.; and (6) a calibrated co-axial line wave-meter (not shown).

[18] Dimroth, *Ber.*, 1901, **34**, 221.
[19] Buckingham, Chau, Freeman, Le Fèvre, Rao, and Tardif, *J.*, 1956, 1405.

TABLE 6. *Dependence of incremental* tan δ *on concentration.*

Solvent	$10^5 w_2$	Δf (Mc./sec.)	$10^3 \Delta$ tan δ
Solute: *Nitrobenzene*			
Dioxan	0	0·98	—
	211	2·30	5·27
	579	4·61	14·48
	0	1·18	—
	242	2·69	5·98
	396	3·65	9·82
p-Xylene	0	0·61	—
	246	1·60	3·93
	452	2·32	6·80
	537	2·75	8·51
	730	3·60	11·92
	847	3·97	13·33
CCl_4	0	0·65	—
	120	1·48	3·31
	273	2·52	7·45
	274	2·57	7·59
	336	2·98	9·26
	0	0·72	—
	377	3·24	10·04
	412	3·70	11·82
	0	0·62	—
	128	1·53	3·62
	262	2·49	7·44
Benzene	0	0·57	—
	356	1·71	4·55
	510	2·29	6·86
	756	3·04	9·85
	0	0·55	—
	205	1·18	2·51
	410	1·89	5·34
	708	2·81	9·01
	0	0·59	—
	249	1·39	3·19
	548	2·43	7·34
	845	3·46	11·45
Toluene	0	2·33	—
	410	3·57	4·91
	503	3·80	5·85
	683	4·30	7·84
	0	2·24	—
	419	3·38	4·55
	678	4·22	7·87
cyclo-C_6H_{12}	0	1·53	—
	1565	5·43	15·55
	2003	6·60	20·21
	2240	7·60	24·60
n-C_7H_{16}	0	0·80	—
	481	1·58	3·11
	761	2·02	4·86
	0	1·90	—
	632	1·90	4·15
	880	2·34	5·70
n-C_6H_{14}	0	0·62	—
	288	1·03	1·64
	580	1·54	3·67
	762	1·79	4·67
	0	0·59	—
	663	1·63	4·14
	1383	2·64	8·14
	1839	3·26	10·63
Solute: 1-*Nitronaphthalene*			
Dioxan	0	2·20	—
	787	6·13	15·67
	848	6·40	16·75
	1490	9·30	28·35
p-Xylene	0	0·80	—
	276	1·91	4·42

Solvent	$10^5 w_2$	Δf (Mc./sec.)	$10^3 \Delta$ tan δ
Solute: 1-*Nitronaphthalene*			
p-Xylene	305	1·97	4·66
	432	2·59	7·12
	0	0·86	—
	171	1·57	2·84
CCl_4	0	0·61	—
	103	1·45	3·35
	155	1·87	5·03
	256	2·80	8·70
C_6H_6	0	0·63	—
	403	2·12	5·94
	541	2·66	8·10
	553	2·65	8·06
	604	2·88	8·97
	740	3·41	11·09
	0	0·65	—
	396	2·17	6·06
	555	2·82	8·65
PhMe	0	2·04	—
	208	2·81	3·06
	398	3·49	5·76
	0	2·23	—
	338	3·47	5·32
	424	3·90	6·57
cyclo-C_6H_{12} ...	0	0·63	—
	386	1·76	4·49
	456	2·02	5·42
	682	2·60	7·84
n-C_7H_{16}	0	0·81	—
	483	1·81	3·99
	903	2·66	7·37
	0	0·77	—
	524	1·87	4·38
	885	2·59	7·25
n-C_6H_{14}	0	0·61	—
	342	1·30	2·74
	386	1·41	3·19
	522	1·70	4·33
Solute: 4-*Nitrodiphenyl*			
Dioxan	0	2·08	—
	231	3·22	4·54
	292	3·54	5·82
	309	3·70	6·46
p-Xylene	0	0·75	—
	316	2·19	5·75
	466	2·78	8·09
	0	0·70	—
	137	1·42	2·90
	446	2·64	7·72
CCl_4	0	1·63	—
	410	4·80	12·64
	414	49·4	13·19
	463	5·24	14·38
	0	1·61	—
	287	3·79	8·69
	437	5·08	13·83
	493	5·24	14·47
C_6H_6	0	0·64	—
	250	1·90	5·02
	331	2·30	6·60
	649	3·88	12·96
	0	0·57	—
	277	1·95	5·50
	421	1·65	8·30
	721	4·17	14·36
	0	0·66	—
	168	1·49	3·31
	263	1·99	5·31

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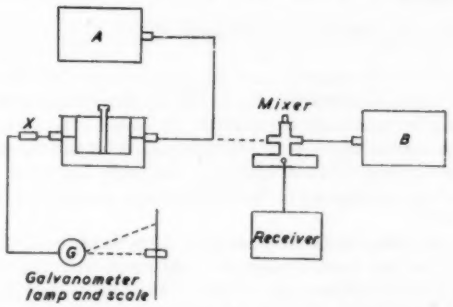
TABLE 6. (*Continued.*)

Solvent	$10^5 w_2$	Δf (Mc./sec.)	$10^3 \Delta \tan \delta$
Solute: 9-*Nitroanthracene*			
p-Xylene	0	1·79	—
	230	2·51	2·77
	498	3·21	5·59
	530	3·27	5·70
	671	3·69	7·32
	1216	5·32	13·62
CCl_4	0	1·79	—
	149	2·58	3·05
	219	3·00	4·67
	341	3·68	7·28
C_6H_6	0	1·52	—
	275	2·30	3·12
	566	3·18	6·28
	836	3·97	9·46
n-C_7H_{16}	0	1·82	—
	134	1·92	0·54
	168	2·01	0·73
	242	2·11	1·12
	307	2·21	1·46
	321	2·25	1·66
Solute: *Benzophenone*			
C_6H_6	0	1·80	—
	655	2·87	4·27
	684	2·90	4·36
	700	2·94	4·54
	780	2·95	4·59
	802	3·01	4·82
	902	3·10	5·22
	911	3·30	5·97
	1165	3·72	7·65
Solute: *Fluorenone*			
C_6H_6	0	1·52	—
	694	3·07	6·18
	714	3·11	6·34
	1006	3·79	9·05
	0	1·58	—
	699	3·14	6·22
	725	3·15	6·26
	1153	4·03	9·77
	0	1·65	—
	781	3·41	7·01
	966	3·77	8·44
Solute: *Pyridine*			
CCl_4	0	1·24	—
	204	2·06	3·16
	595	2·68	5·56
	633	2·76	5·86
	0	1·57	—
	613	3·03	5·63
	931	3·35	6·86
	1221	4·20	10·14
	0	1·74	—
	2049	5·20	13·36
	2664	6·34	16·06
C_6H_6	0	1·64	—
	914	2·22	2·25
	0	1·67	—
	1813	2·84	4·51
	2235	3·18	5·83
	2376	3·46	6·91
n-C_7H_{16}	0	1·81	—
	869	1·98	0·672
	871	2·05	0·936
	964	2·06	0·972
	0	1·71	—

Solvent	$10^5 w_2$	Δf (Mc./sec.)	$10^3 \Delta \tan \delta$
Solute: *Pyridine*			
n-C_7H_{16}	1900	2·20	1·88
	2013	2·25	2·08
	2236	2·40	2·66
Solute: *Quinoline*			
CCl_4	0	1·80	—
	537	2·95	4·44
	620	3·65	7·14
	0	1·88	—
	590	3·29	5·44
	679	3·52	6·32
	787	3·76	7·25
C_6H_6	0	1·71	—
	745	2·41	2·66
	1025	2·66	3·62
	1326	3·09	5·29
	0	1·79	—
	754	2·51	2·77
	908	2·73	3·63
	1471	3·10	5·03
n-C_7H_{16}	0	1·62	—
	1713	2·26	2·47
	2044	2·45	3·20
	2392	2·76	4·39
Solute: iso*Quinoline*			
CCl_4	0	1·80	—
	446	3·85	7·91
	769	4·55	10·61
	917	5·62	14·74
	0	1·20	—
	1924	10·1	34·34
	2013	10·5	35·88
	2254	11·1	38·20
C_6H_6	0	1·67	—
	664	2·90	4·74
	679	2·92	4·82
	1273	3·84	8·34
	0	1·69	—
	1277	4·13	9·42
	1489	4·59	11·20
	1772	4·87	12·28
n-C_7H_{16}	0	1·63	—
	1376	2·58	3·67
	1442	2·68	4·06
	2196	3·29	6·41
Solute: *Acridine*			
CCl_4	0	1·86	—
	186	2·35	1·90
	425	3·05	4·60
	779	3·74	7·26
	0	1·76	—
	813	3·75	7·68
	840	4·00	8·64
	963	4·30	9·80
	0	1·70	—
	759	3·67	7·60
	1055	4·55	11·00
C_6H_6	0	1·68	—
	889	2·73	4·06
	935	2·75	4·13
	1558	3·53	7·14
	0	1·70	—
	1306	3·12	5·47
	1626	3·56	7·18
	1708	3·75	7·91

Both oscillators and the receiver are run for 1 hr. to reach frequency stability; meanwhile the resonator (kept in a desiccator when not in use) is polished with a soft cloth, and a series of solutions made up. The most concentrated solution is put into the quartz tube [14] so that its level is above the resonator lid. The frequency of *A* is then varied across the point of resonance,



galvanometer deflections against frequency vernier settings being recorded. From the resulting plot the frequency vernier settings corresponding to the maximum and the two half-heights on each side of the maximum are obtained (f_r, $f_{y/2}'$ and $f_{y/2}''$ respectively).

The vernier is now reset on f_r and the coaxial cable from *A* connected to the wave-meter (instead of the resonator). This gives f_r directly (it is always *ca.* 3109 Mc./sec.). Next, with

TABLE 7. *Calculation of observed relaxation times.*

Solvent	μ (D) *	ψ_{mean}	Temp.	$10^{12}\tau$ (sec.)
Nitrobenzene				
Dioxan ...	3·910	2·49	295°	21
p-Xylene...	3·917	1·57	290	14
CCl_4	3·925	2·84	295	14
C_6H_6	3·967	1·31	298	11
PhMe	3·83	1·15	295	11
cyclo-C_6H_{12}	3·972	1·00	388	9·3
n-C_7H_{16} ...	4·10	0·65	288	6·4
n-C_6H_{14} ...	4·038	0·62	298	6·8
1-*Nitronaphthalene*				
Dioxan ...	3·90	1·94	288	23
p-Xylene...	(4·0)	1·61	389	21
CCl_4	4·00	3·32	290	25
C_6H_6	3·98	1·50	298	20
PhMe	3·87	1·53	289	21
cyclo-C_6H_{12}	(4·0)	1·16	290	16
n-C_7H_{16} ...	(4·0)	0·82	290	14
n-C_6H_{14} ...	(4·0)	0·82	290	13
4-*Nitrodiphenyl*				
Dioxan ...	4·16	2·02	288	25
p-Xylene...	(4·4)	1·77	288	23
CCl_4	4·39$_5$	3·09	290	21
C_6H_6	4·36	1·99	298	30
9-*Nitroanthracene*				
p-Xylene...	(3·4)	1·11	288	30
CCl_4	3·71	2·12	287	23
C_6H_6	3·43	1·12	285	28
n-C_7H_{14} ...	(3·7)	0·47	286	11
Benzophenone				
C_6H_6	2·7	0·63	298	19·2 (or 136)
Fluorenone				
C_6H_6	3·35	0·88	298	17·0 (or 156)
Pyridine				
CCl_4	2·37	0·88	288	7·2
C_6H_6	2·25	0·27	286	4·4
n-C_7H_{16} ...	2·27	0·10	287	2·2
Quinoline				
CCl_4	2·27	0·95	288	14
C_6H_6	2·24	0·37	287	10
n-C_7H_{16} ...	2·17	0·16	287	6·0
iso*Quinoline*				
CCl_4	2·65	1·70	288	21
C_6H_6	2·61	0·71	286	15
n-C_7H_{16} ...	2·60	0·28	287	7·2
Acridine				
CCl_4	2·22	1·01	288	26
C_6H_6	2·18	0·45	287	20

* Dipole moments for nitrobenzene are from Smith and Cleverdon (*Trans. Faraday Soc.*, 1949, **45**, 109) when shown as four figures, otherwise from the M.I.T. Tables. Remaining data come from the following paper or from refs. 19 and 20. Values in parentheses are assumed.

the vernier at $f_{y/2}'$, the cable from *A* is joined to the mixer (broken line in Figure) so that the output from *A* combines with that from *B*, which is adjusted until a beat-note starts to be

[19] Hughes, Le Fèvre, and Le Fèvre, *J.*, 1937, 202.

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heard in the loud speaker. The mixer is then tuned until the signal is a maximum. The receiver dial reading is then noted. A repetition with the frequency vernier of A at $f_{y/2}''$ then gives another receiver reading, the difference of which from the first is the desired Δf. The Q factor of the system is $f_r/\Delta f$. The same procedure is followed for the other solutions, and for the solvent. Then we have:

$$\Delta \tan \delta = (\text{constant})(1/Q_{12} - 1/Q_1)$$

where the constant may be determined from the geometry of the resonator, or more conveniently, from a series of measurements on liquids or solutions having known values of $\Delta \tan \delta$. Subsequent computation is based upon equation (5) of ref. 16, ψ being a mean obtained as $\Sigma(\Delta \tan \delta/\Sigma w_2)$. Solvent constants ($D$ in ref. 16) appropriate for the temperature range commonly experienced are given in Table 5 for those media not listed by Le Fèvre and Sullivan;[16] Table 6 records the experimental quantities requisite to secure the values of ψ, and Table 7 presents the relaxation times now found.

Tables 6 and 7 include data for benzophenone. This solute was chosen as a "standard" because its relaxation time has been measured at different frequencies and temperatures; in benzene τ undoubtedly lies [2, 14] between 16 and 21 $\times$ 10^{-12} sec. Now by the nature of equation 5 given by Le Fèvre and Sullivan [16] τ is extracted from observations as a pair of values, one high and one low. As we lacked equipment working at a second wavelength we could not select τ by experiment directly in cases where the larger τ might have been correct (*e.g.*, with 4-nitrodiphenyl). Accordingly τ for benzophenone emerged as 19 or 136 $\times$ 10^{-16} sec.—a pair of values resembling in magnitude those experienced with several other of the larger solutes. Since the lower figure is appropriate for benzophenone we assumed the same to be true in the remaining doubtful instances; Tables 4 and 7 have been compiled on this basis.

Fluorenone was added for interest: its aromatic rings [20] must be held rigidly in contrast to those of benzophenone; this important structural difference does not seriously affect the observed relaxation times.

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442. *Dielectric Polarisation of 1-Nitronaphthalene, 9-Nitroanthracene, and 4-Nitrodiphenyl in Various Solvents.*

By J. Y. H. CHAU and R. J. W. LE FÈVRE.

The magnitudes of the apparent orientation polarisations of the solutes in the title in dioxan, carbon tetrachloride, or benzene are not in the order predicted by earlier empirical equations for solvent effects.

THE dielectric polarisations now reported were observed in connection with the work of the preceding paper. We present them separately because of their bearing on the problem of solvent effects in dipole moment measurements.

Barclay and Le Fèvre [1] and Buckingham and Le Fèvre [2] tested their equations (connecting the ratios ${}_0P_{\text{soln.}}/{}_0P_{\text{gas}}$ between the apparent and true orientation polarisations of a dissolved species with shape and solvent properties) with the ${}_0P_{\text{soln.}}$ figures published by Cleverdon and Smith [3] for nitrobenzene in various media. A minor disagreement was noted. In benzene, carbon tetrachloride, and dioxan, the observed orientation polarisations increased from dioxan to benzene, whereas predictions based on equations numbered 1 to 4 by Buckinghan and Le Fèvre [2] suggested the reverse, as annexed.

[1] Barclay and Le Fèvre, *J.*, 1950, 556.
[2] Buckingham and Le Fèvre, *J.*, 1952, 1932.
[3] Cleverdon and Smith, *Trans. Faraday Soc.*, 1949, **45**, 109.

Ratios $_{0}P_{soln.}/_{0}P_{gas}$ *for nitrobenzene.*

Reqd. by equation	1	2	3	4	Expt.
Dioxan	0·88	0·91	0·90	0·89	0·85
Carbon tetrachloride	0·86	0·88	0·87	0·89	0·86
Benzene	0·85	0·87	0·85	0·88	0·87

It was therefore of interest to ascertain how the orientation polarisations of other nitroaryls are graded in these three solvents. The results are given in Tables 1—3.

TABLE 1. *Solvent constants at 25°.*

	ε	d_4^{25}	p_1 (c.c.)	$C = 3M_1/d_1(\varepsilon_1 + 2)^2$
Carbon tetrachloride	2·2270	1·58454	0·18319	0·10596
Dioxan	2·2090	1·0280	0·2794	0·1647
Benzene	2·2725	0·87378	0·34086	0·18809
Toluene	2·3661	0·8622	0·3629	0·1825

TABLE 2. *Dielectric constant and density measurements.*

10^5w_2	ε_{25}	d_4^{25}	10^5w_2	ε_{25}	d_4^{25}
1-Nitronaphthalene in dioxan					
840	2·3029	1·0295	1173	2·3392	1·0300
954	2·3154	1·0296	1174	2·3441	1·0301
990	2·3226	1·0299			
1-Nitronaphthalene in carbon tetrachloride					
343	2·2901	1·5828	579	2·3325	1·5815
510	2·3205	1·5820	1057	2·4209	—
563	2·3309	1·5819	1844	2·5653	—
1-Nitronaphthalene in benzene					
800	2·3555	0·8763	945	2·3698	0·8770
864	2·3628	0·8766	965	2·3705	0·8771
908	2·3665	0·8768	1140	2·3919	0·8774
1-Nitronaphthalene in toluene					
555	2·4201	0·8639	1248	2·4904	0·8656
814	2·4464	0·8644	1390	2·5041	0·8660
1058	2·4722	0·8650	1553	2·5210	0·8665

10^5w_2	ε_{25}	d_4^{25}	10^5w_2	ε_{25}	d
9-Nitroanthracene in carbon tetrachloride					
75	2·2353	1·58320	94	2·2379	1·58286
84	2·2367	1·58306	128	2·2415	—
94	2·2374	1·58291			
9-Nitroanthracene in benzene					
268	2·2890	—	481	2·3020	0·8750
275	2·2894	—	493	2·3034	0·8751
312	2·2915	0·8746	566	2·3079	0·8753
325	2·2920	0·8746	836	2·3251	0·8761
384	2·2959	0·8747			
4-Nitrodiphenyl in dioxan					
270	2·2395	1·0283	519	2·2665	1·0286
317	2·2441	1·0284	579	2·2731	1·0287
475	2·2612	1·0285	588	2·2740	1·0288
4-Nitrodiphenyl in carbon tetrachloride					
121	—	1·58368	204	—	1·58310
123	2·2503	—	207	2·2654	—
136	—	1·58343	209	2·2657	—
139	2·2530	—	227	2·2702	1·58284
188	2·2630	—	302	2·2838	1·58216
190	2·2635	—	303	2·2853	—

TABLE 3. *Calculations of dipole moments.*

Solute	Solvent	$d\varepsilon_1$	β	$_{\infty}P_2$ (c.c.)	R_D (c.c.)	μ (D)
1-Nitronaphthalene	Dioxan	11·29	$0·172_5$	362·1	50·1 *	3·90
,,	CCl_4	$18·33_5$	−0·315	378·2	,,	4·00
,,	Benzene	10·35	0·378	373·9	,,	3·98
,,	Toluene	$9·93_7$	0·319	356·9	,,	3·87
9-Nitroanthracene	CCl_4	(11·33)	(−1·111)	(354·3)	72·7 *	(3·71)
,,	Benzene	$6·18_5$	0·301	312·9	,,	3·43
4-Nitrodiphenyl	Dioxan	11·08	0·117	412·7	58·1 *	4·16
,,	CCl_4	18·92	$-0·477_5$	453·3	,,	$4·39_5$

* Computed from R_D of the parent hydrocarbon by taking R_D values of 1·03 and 6·71 c.c. respectively for H and NO_2 (see Vogel, *J.*, 1948, 1833; Campbell, Le Fèvre, Le Fèvre, and Turner, *J.*, 1938, 404).

1-Nitronaphthalene and 4-nitrodiphenyl have been examined hitherto only in benzene; Wesson [4] gives $\mu = 3·62$ or 3·88 D for the former and 4·17 or 4·28 D for the latter. Our figures for 1-nitronaphthalene (3·98 D) in benzene is identical with one reported by Vassiliev and Sirkin.[5] No previous determinations of the moment of 9-nitroanthracene appear to be recorded; the material is sparingly soluble in carbon tetrachloride and our

[4] Wesson, "Tables of Electric Dipole Moments," Technology Press, Massachusetts Institute of Technology, 1948.

[5] Vassiliev and Sirkin, *Acta Physicochim. U.S.S.R.*, 1941, **14**, 414.

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results (Table 3, and below) in this medium, being therefore somewhat uncertain, are shown in parentheses.

Littlejohn and Smith [6] have published data for 4-nitrodiphenyl in benzene ($_{\infty}P_2 = 447{\cdot}7$ c.c. at 25°, $\mu = 4{\cdot}36$ D) which seem concordant with ours in carbon tetrachloride.

The following solvent actions on $\mu_{apparent}$ can accordingly be discerned: for 1-nitronaphthalene and 4-dinitrodiphenyl μ increases in order dioxan < benzene < carbon tetrachloride and for nitrobenzene the order is dioxan < carbon tetrachloride < benzene (for 9-nitroanthracene μ is less in benzene than in carbon tetrachloride). The order for nitrobenzene is contrary to that predicted. Since no information is available for n_2 for the present solutes at 25°, Buckingham and Le Fèvre's equations cannot be applied. As an approximation, however, the shape factors A, B, and C from the previous paper have been applied in the rough form: $\mu_s^2/\mu_g^2 = 1 + (\varepsilon_1 - 1)(\exp x^2 - 1)/(\varepsilon_1 + 2)$ to compute ratios μ_{s1}^2/μ_{s2}^2. Predictions for 1-nitronaphthalene, 9-nitroanthracene, or 4-nitrodiphenyl, however, again resemble those for nitrobenzene, *viz.*, the apparent moments should be greatest in dioxan and least in benzene: by experiments the expected order is observed only in carbon tetrachloride and benzene, being less in dioxan than either of the others.

Experimental.—The solutes were recrystallised specimens with m. p.s given in Beilstein's "Handbuch." Experimental procedures and methods of calculation were those described by Le Fèvre; [7] the circuit used to determine ε was that noted by Buckingham *et al.*[8] For symbols used see ref. 7.

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[6] Littlejohn and Smith, *J.*, 1953, 2456.
[7] Le Fèvre, "Dipole Moments," Methuen, London, 3rd Edn., 1953, Chap. 2.
[8] Buckingham, Freeman, Le Fèvre, Narayana Rao, and Tardif, *J.*, 1956, 1405.

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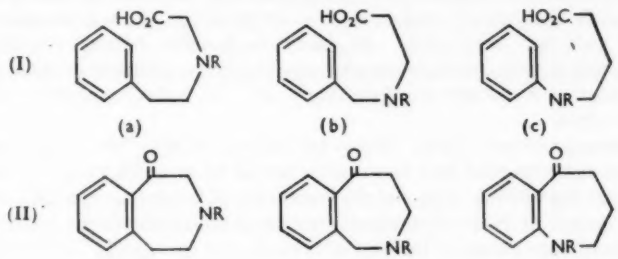
443. *Azabenzocycloheptenones. Part I. The Friedel–Crafts Reaction with Aryl-amino-acids.*

By G. R. PROCTOR and R. H. THOMSON.

For various reasons the aryl-amino-acids (Ia, b, and c) do not, in general, cyclise to azabenzo*cyclo*heptenones although the ketone (IIa; R = *p*-$C_6H_4Me{\cdot}SO_2$) can be detected after treatment of the chloride of (Ia; R = *p*-$C_6H_4Me{\cdot}SO_2$) with aluminium chloride in carbon disulphide at a low temperature. The glycine (Ia; R = *p*-$C_6H_4Me{\cdot}SO_2$) loses carbon monoxide when heated in polyphosphoric acid and cyclises to a tetrahydro-*iso*quinoline. β-Benzylaminopropionic acids (Ib) are readily debenzylated and a variety of products is formed under Friedel–Crafts conditions. β-(3 : 4-Dimethoxybenzylamino)propionic acid readily undergoes β-elimination of the amine under acid conditions. Attempts to cyclise the γ-anilinobutyric acid (Ic; R = *p*-$C_6H_4Me{\cdot}SO_2$) or to form its acid chloride gave a lactam, with displacement of the toluene-*p*-sulphonyl group, and if the benzene ring was activated by methoxyl groups toluene-*p*-sulphonation occurred in that ring when the reaction was conducted in polyphosphoric acid. Other examples of $N \longrightarrow C$ migration of a toluene-*p*-sulphonyl group have been found. Anisole is acylated by toluene-*p*-sulphonic acid in polyphosphoric acid.

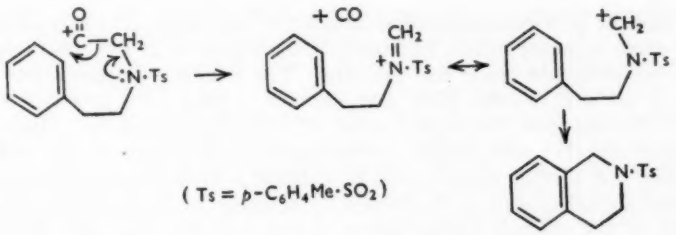
ALL three azabenzo*cyclo*heptenes containing nitrogen in the seven-membered ring have been known for many years but none of the simple azabenzo*cyclo*heptenones (apart from

lactams) had been obtained when this work began (one has since been prepared [1]). The cyclisation of the aryl-amino-acids (Ia, b, and c) appears to be an obvious route to them. We have found, however, that in general, but for different reasons, these three types of



acid do not cyclise to the ketones (II). In studying these reactions the toluene-*p*-sulphonyl group was selected for protection of the amino-group as this has been found satisfactory [2] (in contrast to other acyl groups [3]) in analogous quinolone syntheses; the use of *N*-alkyl groups was avoided as these would be more difficult to remove subsequently.

N-2′-*Arylethylglycines* (Ia).—Cyclisation of this type of acid has been studied by von Braun and his co-workers: by heating the acid (Ia; R = Ph·SO_2) with phosphoric oxide [4] in boiling xylene, or by treating its chloride with aluminium chloride [5] in nitrobenzene in the cold, they obtained *N*-benzenesulphonyl-1 : 2 : 3 : 4-tetrahydro*iso*quinoline with the loss of carbon monoxide. Tetrahydro-*N*-methyl*iso*quinoline was obtained likewise from the chloride of (Ia; R = Me).[6] No ketones (IIa) were detected but an azabenzo*cyclo*heptene was obtained by extending the reaction to the cyclisation of the homologous *N*-benzenesulphonyl-*N*-3′-phenylpropylglycine.[4, 6] We found, similarly, that heating the acid (Ia; R = *p*-C_6H_4Me·SO_2) in polyphosphoric acid yielded 1 : 2 : 3 : 4-tetrahydro-*N*-toluene-*p*-sulphonyl*iso*quinoline; no reaction occurred in the cold. Tertiary acid



chlorides frequently undergo decarbonylation when treated with aluminium chloride: $RR'R''C{\cdot}CO^+ \longrightarrow RR'R''C^+ + CO$. Rothstein and Saville [7] have shown that elimination of carbon monoxide from the intermediate carbonium ion is assisted by electron-release from the alkyl groups to which it is attached, and a parallel mechanism can be envisaged for the amino-acid reactions, decarbonylation being initiated by electron release from the adjacent nitrogen atom. This apparently occurs even when the group Ar·SO_2

[1] Astill and Bockelheide, *J. Amer. Chem. Soc.*, 1955, **77**, 4080; cf. Braunholz and Mann, *Chem. and Ind.*, 1957, 266.
[2] Clemo and Perkin, *J.*, 1924, **125**, 1608; Johnson, Woroch, and Buell, *J. Amer. Chem. Soc.*, 1949, **71**, 1901; Elderfield and Maggiolo, *ibid.*, 1949, **71**, 1906.
[3] Elderfield, Gensler, Bembry, Kremer, Brody, Hageman, and Head, *ibid.*, 1946, **68**, 1259.
[4] von Braun and Bayer, *Ber.*, 1927, **60**, 1262.
[5] von Braun, Blessing, and Cahn, *Ber.*, 1924, **57**, 910.
[6] von Braun and Wirz, *ibid.*, 1927, **60**, 102.
[7] Rothstein and Saville, *J.*, 1949, pp. 1946, 1950, 1954, 1959, 1961.

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is attached to it. To some extent it is possible to influence the competition between the acylation and decarbonylation by temperature control and we found that by treating the acid chloride of (Ia; R = *p*-$C_6H_4Me{\cdot}SO_2$) with aluminium chloride in carbon disulphide at 0°, or lower, some ketone (IIa; R = *p*-$C_6H_4Me{\cdot}SO_2$) was formed (along with the tetrahydro*iso*quinoline derivative) and it was isolated as its 2 : 4-dinitrophenylhydrazone. However the yield was very small. It should be possible to improve this reaction by using an acid with a more reactive benzene nucleus, but a preliminary trial with *N*-3′ : 4′-dimethoxyphenethyl-*N*-toluene-*p*-sulphonylglycine in polyphosphoric acid gave an intractable product.

β-*Benzylaminopropionic Acids* (Ib).—As benzyl groups are easily detached from nitrogen it was not expected that these acids would be of much value in the synthesis of the azabenzo*cyclo*heptenones (IIb) and we found that *N*-benzyl-amides and -sulphonamides (with the exception of *N*-4′-nitrobenzylbenzenesulphonamide) were readily split in hot benzene by aluminium chloride, the products being the free amide and diphenylmethane :

$$Ph{\cdot}CH_2{\cdot}\underset{\cdot\cdot}{N}R{\cdot}SO_2{\cdot}Ar \longrightarrow Ph{\cdot}CH_2\overset{\curvearrowright}{-}\overset{+}{N}R{\cdot}SO_2{\cdot}Ar \longrightarrow Ph{\cdot}CH_2{\cdot}Ph + HNR{\cdot}SO_2{\cdot}Ar$$
$$\qquad\qquad\qquad\qquad\qquad\qquad\quad |$$
$$\qquad\qquad\qquad\qquad\qquad\qquad\quad {}^-AlCl_3$$

Various attempts to cyclise the acid (Ib; R = *p*-$C_6H_4Me{\cdot}SO_2$) or its chloride were unsuccessful but signs of fragmentation were plentiful, *e.g.*, treatment with phosphoric oxide in benzene yielded some diphenylmethane. Only when the acid chloride (III) was treated with aluminium chloride in benzene was ketonic material (IV) isolated. The other products of the reaction are as shown.

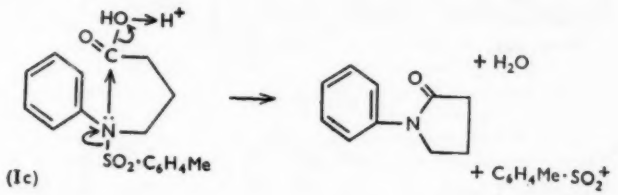
$$\underset{\text{(III)}}{Ph{\cdot}CH_2{\cdot}NTs{\cdot}CH_2{\cdot}CH_2{\cdot}COCl} \longrightarrow Ph{\cdot}CH_2{\cdot}Ph + \underset{\text{(IV)}}{NHTs{\cdot}CH_2{\cdot}CH_2{\cdot}COPh} + H_2N{\cdot}Ts$$
$$+$$
$$[Ph{\cdot}CH_2{\cdot}C_6H_4{\cdot}CO{\cdot}CH_2{\cdot}CH_2{\cdot}NHTs] \quad \text{(V)}$$

Like a number of *N*-monoalkylsulphonamides,[8,9] the amide (IV) is insoluble in alkali but in hot dilute aqueous sodium hydroxide it was degraded to toluene-*p*-sulphonamide, a trace of benzaldehyde being also detected. The toluene-*p*-sulphonamide formed on treatment of the acid chloride (III) with aluminium chloride is probably a secondary product also derived from the sulphonamide (IV) by a β-elimination. Oxidation of the pure sulphonamide (IV) with alkaline permanganate yielded benzoic acid and toluene-*p*-sulphonamide, but a crude sample gave in addition a little *p*-benzoylbenzoic acid, presumably from a product such as (V) formed by acylation of the diphenylmethane.

Reaction of the chloride hydrochloride of the acid (Ib; R = H) with aluminium chloride in benzene gave the ketone $Ph{\cdot}CH_2{\cdot}NH{\cdot}CH_2{\cdot}CH_2{\cdot}COPh$, previously obtained by a Mannich reaction,[10] but intramolecular acylation could not be achieved in inert solvents; β-elimination of benzylamine usually occurred and again traces of benzaldehyde were formed. Easy β-elimination also defeated attempts to utilise β-(3 : 4-dimethoxybenzylamino)propionic acid; on treatment in polyphosphoric acid this liberates veratrylamine even in the cold. In one experiment a minute yield of oil was isolated which formed a 2 : 4-dinitrophenylhydrazone. According to its analysis (C and H) it could be the azabenzo*cyclo*heptenone (IIb) but the results could not be repeated. During the toluene-*p*-sulphonylation of β-3 : 4-dimethoxybenzylpropionic acid some *N*-3 : 4-dimethoxybenzyltoluene-*p*-sulphonamide was formed and the latter also arose when the toluene-*p*-sulphonamido-acid was treated with polyphosphoric acid.

[8] Briscoe, Challenger, and Duckworth, *J.*, 1956, 1755.
[9] Carothers, Bickford, and Hurwitz, *J. Amer. Chem. Soc.*, 1927, **49**, 2913.
[10] Mannich and Hieronimus, *Ber.*, 1942, **75**, 61.

γ-Arylaminobutyric Acids (Ic).—The parent acid (Ic; R = H) is unknown and attempts to prepare it led to the corresponding lactam, 1-phenyl-2-pyrrolidone. The *N*-toluene-*p*-sulphonyl derivative was obtained by interaction of *N*-toluene-*p*-sulphonylaniline and ethyl γ-bromobutyrate, followed by cold alkaline hydrolysis. Attempted cyclisation of the toluene-*p*-sulphonamido-acid (Ic) in polyphosphoric acid yielded only 1-phenylpyrrolid-2-one and reaction with thionyl chloride, phosphorus pentachloride, or phosphorus oxychloride yielded, not the expected acid chloride, but a mixture of the pyrrolidone



(Ic)

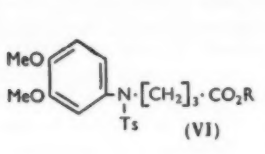
and toluene-*p*-sulphonyl chloride. When these experiments were complete Astill and Bockelheide [1] published essentially the same results but they inferred that reaction of the acid (Ic; R = *p*-$C_6H_4Me{\cdot}SO_2$) with phosphorus pentachloride gave the corresponding acid chloride. However we found that hydrolysis of the product obtained by treatment of the acid with thionyl chloride gave only pyrrolidone and none of the starting acid was recovered. The existence of the chloride of (Ic; *p*-$C_6H_4Me{\cdot}SO_2$) is highly improbable. This appears to be generally true of γ-amino-acids, even those containing tertiary amino-groups (cf. Wilson [11]), and is reminiscent of the alleged acid chlorides of α-acylamino-acids which are in fact oxazolone hydrochlorides.[12]

Finally the acid (VI; R = H) was examined in the hope that the methoxyl groups would promote acylation of the benzene ring. This proved to be the case, but not as expected, for heating in polyphosphoric acid gave a neutral product which we regard as the pyrrolidone (VII; R = *p*-$C_6H_4Me{\cdot}SO_2$) rather than the azabenz*o*cyclo*hepten*one (VIII), the toluene-*p*-sulphonyl group having migrated to an *ortho*-position (2 or 6) in the benzene ring. This compound is devoid of ketonic properties and its infrared spectrum shows a carbonyl band at 1705 cm.$^{-1}$ (in CCl_4) [cf. ν'_{CO} for 1-phenylpyrrolidone, its dimethoxy-derivative (VII; R = H), and the ketone (VIII; H in place of OMe) (see following paper) which lie at 1708, 1700, and 1688 cm.$^{-1}$ respectively in CCl_4]. On the other hand, the pyrrolidone (VII; R = H) was obtained when the acid (VI; R = H) was treated with cold hydrogen fluoride or with hot phosphoric oxide or, along with toluene-*p*-sulphonyl chloride, on reaction with thionyl chloride. We have shown that an activated benzene ring (anisole) is acylated by toluene-*p*-sulphonic acid in hot polyphosphoric acid although we have not succeeded in acylating the pyrrolidone (VIII; R = H) under these conditions. This is possibly accounted for by a steric factor which does not operate during the conversion of the acid (VI; R = H) into the pyrrolidone (VII; R = *p*-$C_6H_4Me{\cdot}SO_2$) when the approaching carbonyl group simultaneously displaces the toluene-*p*-sulphonyl group from the rear of the nitrogen atom whence it can migrate to an *ortho*-position unimpeded. Conversely, once this group is attached to the benzene ring formation of a lactam is difficult. Heating the ester (VI; R = Et) for 10 minutes in polyphosphoric acid gave the isomer (IX; R = Et), showing infrared bands at 3406 (NH) and 1729 cm.$^{-1}$ (ester C:O). Alkaline hydrolysis afforded the acid (IX; R = H) which was also obtained by heating the acid (VI; R = H) in stannic chloride. The acid (IX; R = H) did not form a lactam in hot polyphosphoric acid.

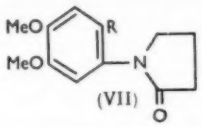
[11] Wilson, *J.*, 1952, 3524.
[12] Cornforth, "The Chemistry of Penicillin," Princeton Univ. Press, 1949, p. 731.

XUM

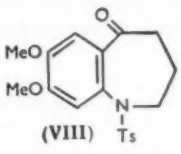
Similar $N \longrightarrow C$ migrations have been noted by Mustafa and Ali [13] who found that the toluene-*p*-sulphonyl group in the naphthasultam (X), and one of the groups in *NN*-di-toluene-*p*-sulphonylaniline, migrated to the *para*-position in the presence of aluminium chloride. Johnson, Woroch, and Buell [2] noted the formation of phenyl *p*-tolyl sulphone during cyclisation of the chloride of (XI; R = H, R′ = Cl) with aluminium chloride in



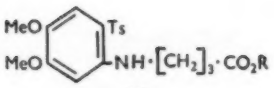
(VI)



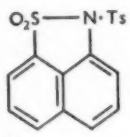
(VII)



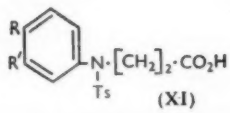
(VIII)



(IX)

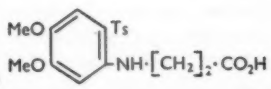


(X)



(XI)

(Ts = *p*-$C_6H_4Me \cdot SO_2$)



(XII)

benzene and in one experiment it was the main product. We have also found that the acid (XI; R = R′ = OMe) rearranges to (XII) (or the 2-acyl isomer) in hot polyphosphoric acid whereas its chloride undergoes cyclisation (without migration) to a quinolone when treated with stannic chloride in benzene.

Experimental

Microanalysis of a number of sulphonamides in this, and the following paper, gave very erratic results and the figures quoted are, in some cases, the best of several determinations.

N-(2′-Cyanoethyl)benzylamine (cf. ref. 14).—Benzylamine (214 g.) and 40% aqueous potassium hydroxide (5 ml.) were stirred in a cold-water bath while acrylonitrile (106 g.) was added during ½ hr. The solutions was stirred for 5½ hr., poured into water (500 ml.), and extracted with chloroform. The extract was dried an evaporated, and the residue distilled at 174—175°/14 mm. (85%).

*N-Benzyl-β-toluene-*p*-sulphonamidopropionic Acid.*—The above amine (270 g.) and 10% aqueous sodium hydroxide (1 l.) were refluxed together for 3 hr. and then cooled. The homogeneous solution was shaken with toluene-*p*-sulphonyl chloride (340 g.) in ether (1300 ml.) for 6 hr. The aqueous layer was acidified with concentrated hydrochloric acid, kept for 12 hr. at 0°, and filtered. The product was washed with cold water and crystallised from aqueous ethanol in needles, m. p. 130—133° (45%). The m. p. was raised to 136° by crystallisation from ethyl acetate–light petroleum (b. p. 80—90°). The *acid chloride* crystallised from light petroleum (b. p. 80—90°) in needles, m. p. 78° (Found: C, 58·3; H, 5·35; N, 4·0. $C_{17}H_{18}O_3NSCl$ requires C, 58·0; H, 5·1; N, 4·0%). The *amide* (from aqueous ethanol) had m. p. 125° (Found: C, 61·45; H, 6·0; N, 8·2. $C_{17}H_{20}O_3N_2S$ requires C, 61·45; H, 6·0; N, 8·45%). The *anilide* crystallised from the same solvent in needles, m. p. 146° (Found: C, 67·4; H, 5·75; N, 7·0. $C_{23}H_{24}O_3N_2S$ requires C, 67·65; H, 5·9; N, 6·85%). During the preparation of the acid chloride much acidic material was found, insoluble in light petroleum; crystallised from a small volume of water it had m. p. 180—181°; analyses indicate that it is a *monohydrate* of the starting acid (Found: C, 58·15; H, 6·0; N, 3·9; S, 9·1. $C_{17}H_{19}O_4NS,H_2O$ requires C, 58·1; H, 6·0; N, 4·0; S, 9·1%). Acidification of its alkaline solution gave *N*-benzyl-β-toluene-*p*-sulphonamidopropionic acid, m. p. 136°.

[13] Mustafa and Ali, *J. Amer. Chem. Soc.*, 1955, **77**, 4593.
[14] King and McMillan, *ibid.*, 1946, **68**, 1468.

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N-*Toluene*-p-*sulphonyl*-β-*alanine* crystallised from aqueous methanol or ethyl acetate–light petroleum (b. p. 80—90°) in prisms, m. p. 123—124° (Found: C, 49·5; H, 5·25; N, 5·95; S, 13·5. $C_{10}H_{13}O_4NS$ requires C, 49·4; H, 5·4; N, 5·75; S, 13·2%).

ω-*Toluene*-p-*sulphonamidopropiophenone*.—(*a*) β-Toluene-*p*-sulphonamidopropionyl chloride (from 2 g. of the acid) was dissolved in dry benzene (25 ml.), anhydrous aluminium chloride (2 g.) was added, and the mixture refluxed for ½ hr. and left at room temperature for 2 hr. Working up gave the *ketone* as needles, m. p. 110° (74%) (from ethyl acetate–light petroleum) (Found: C, 63·1; H, 5·65; N, 4·75; S, 10·7. $C_{16}H_{17}O_3NS$ requires C, 63·35; H, 5·65; N, 4·6; S, 10·6%). The 2 : 4-*dinitrophenylhydrazone* crystallised from acetic acid–ethanol as orange needles, m. p. 215° (Found: C, 54·4; H, 4·2; N, 14·4; S, 6·8. $C_{22}H_{21}O_6N_5S$ requires C, 54·65; H, 4·4; N, 14·5; S, 6·6%). The *oxime* crystallised from ethyl acetate–light petroleum (b. p. 80—90°) having m. p. 131—132° (Found: C, 60·65; H, 5·4; N, 8·6; S, 10·0. $C_{16}H_{18}O_3N_2S$ requires C, 60·35; H, 5·7; N, 8·8; S, 10·1%). (*b*) *N*-Benzyl-β-toluene-*p*-sulphonamidopropionyl chloride (2·9 g.) in dry benzene (25 ml.) was treated with anhydrous aluminium chloride (3 g.) in portions with shaking, refluxed for 1½ hr., cooled, and treated with crushed ice. The benzene layer was washed successively with dilute hydrochloric acid, dilute aqueous sodium hydroxide, and water, dried ($MgSO_4$), and evaporated under reduced pressure. The residual oil was washed with light petroleum (b. p. 80—90°) and crystallised from the same solvent (charcoal) as needles, m. p. 106° (1 g.). Admixture of this material with authentic ω-toluene-*p*-sulphonamidopropiophenone raised the m. p. to 109—110° (2 : 4-dinitrophenylhydrazone, m. p. and mixed m. p. 215°). From the alkaline washings toluene-*p*-sulphonamide (m. p. and mixed m. p. 137°) was obtained on acidification, and the light petroleum washings contained diphenylmethane, identified as its 4 : 4′-dinitro-derivative, m. p. and mixed m. p. 169°. If the starting material was not pure the yield of ketone was much lower and phenyl *p*-tolyl sulphone (m. p. and mixed m. p. 127°) was obtained in addition to the above.

Oxidation of the pure ketone with alkaline potassium permanganate gave only benzoic acid and toluene-*p*-sulphonamide, but a crude sample gave, in addition, an acid which crystallised from water and had m. p. 196°, alone and mixed with *p*-benzoylbenzoic acid [Found: C, 74·6; H, 4·7%; equiv. (by titration), 210. Calc. for $C_{14}H_{10}O_3$: C, 74·3; H, 4·45%; equiv., 226].

Hydrolysis. The ketone (0·75 g.) was stirred vigorously in a creased flask * with water (200 ml.) and 10% aqueous sodium hydroxide (40 ml.) at 80° for 4 hr. The cooled solution was extracted with chloroform from which a trace of benzaldehyde was isolated (2 : 4-dinitrophenylhydrazone, m. p. and mixed m. p. 235°). Acidification and ether extraction of the alkaline solution afforded toluene-*p*-sulphonamide, m. p. and mixed m. p. 139°.

Debenzylation Experiments.—The general method is illustrated by the following example: *N*-benzyltoluene-*p*-sulphonamide (10 g.) was dissolved in dry benzene (25 ml.), anhydrous aluminium chloride (7 g.) was added, and the mixture heated on the steam-bath for 1 hr. Ice and hydrochloric acid were then added and the mixture was set aside for 2 hr. Toluene-*p*-sulphonamide (4·2 g.), m. p. and mixed m. p. 137°, was collected by filtration and the benzene layer yielded diphenylmethane, b. p. 60—70°/0·05 mm. (3 g.) (4 : 4′-dinitro-derivative, m. p. and mixed m. p. 169°).

Similarly *N*-benzyl-*N*-methyltoluene-*p*-sulphonamide (10 g.) gave diphenylmethane (5 g.) and *N*-methyltoluene-*p*-sulphonamide (3·2 g.); *N*-benzenesulphonylbenzylamine (10 g.) gave diphenylmethane (4·5 g.) and benzenesulphonamide (2·5 g.); *N*-benzoylbenzylamine (10 g.) gave diphenylmethane (5 g.) and benzamide (3 g.); *N*-acetylbenzylamine (20 g.) gave diphenylmethane (3·5 g.) and starting material (8 g.) was recovered (reaction time 3 hr.); *N*-benzenesulphonyl-*p*-nitrobenzylamine was unaffected.

ω-*Benzylaminopropiophenone*.—β-Benzylaminopropionyl chloride hydrochloride [15] (4·5 g.) was suspended in dry benzene (25 ml.), and anhydrous aluminium chloride (3 g.) was added with shaking. The suspension was heated on the steam-bath overnight, cooled, poured on crushed ice and concentrated hydrochloric acid, and left for 2 days. The benzene layer was removed and the aqueous suspension of the amino-ketone hydrochloride filtered. It crystallised from acetone–ethanol in needles, m. p. 165° (13%) (Found: C, 69·3; H, 6·5; N, 5·45; Cl, 13·15. Calc. for $C_{16}H_{18}ONCl$: C, 69·7; H, 6·5; N, 5·1; Cl, 12·9%). The free base separated from

* *I.e.*, a flask in which indentations were made whilst hot.

[15] Fischer, *Ber.*, 1905, **38**, 2917.

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light petroleum (b. p. 80—90°) in prisms, m. p. 70° (lit.,[14] 67°) (Found : N, 5·95. Calc. for $C_{16}H_{17}ON$: N, 5·85%). The *picrate*, m. p. 135°, crystallised from aqueous alcohol (Found : C, 56·65; H, 4·4; N, 11·9. $C_{22}H_{20}O_8N_4$ requires C, 56·4; H, 4·3; N, 11·95%). The 2 : 4-*dinitrophenylhydrazone* separated from ethanol in orange needles, m. p. 196° (Found : N, 15·2. $C_{23}H_{22}O_4ClN_5$ requires N, 15·35%). The *toluene*-p-*sulphonyl derivative* crystallised from light petroleum (b. p. 80—90°) in needles, m. p. 102° (Found : C, 70·1; H, 5·9; N, 3·95; S, 8·2. $C_{23}H_{23}O_3NS$ requires C, 70·2; H, 5·85; N, 3·55; S, 8·15%). The last compound formed a 2 : 4-dinitrophenylhydrazone, orange needles (from acetic acid–ethanol), m. p. 179° (Found : N, 11·7; S, 5·35. $C_{29}H_{21}O_6N_5S$ requires N, 12·2; S, 5·6%).

β-(3 : 4-*Dimethoxybenzylamino*)*propionic Acid*.—A mixture of 3 : 4-dimethoxybenzylamine (62 g.) and 40% aqueous potassium hydroxide (2·5 ml.) was treated with acrylonitrile (20 g.) as before. *N*-2′-Cyanoethyl-3 : 4-dimethoxybenzylamine distilled at 171°/0·05 mm. (52 g., 64%). This nitrile (52 g.) and 10% aqueous sodium hydroxide (350 ml.) were refluxed for 3 hr., cooled, neutralised with hydrochloric acid, and evaporated to dryness in a vacuum on the steam-bath. The solid residue was repeatedly extracted with absolute ethanol from which the colourless acid separated (after several days at 0°), having m. p. 150° (44 g., 78%) (Found : C, 59·85; H, 7·15; N, 5·85. $C_{12}H_{17}O_4N$ requires C, 60·25; H, 7·1; N, 5·85%).

The *toluene*-p-*sulphonyl derivative* had m. p. 103° (from aqueous ethanol) (Found : C, 57·75; H, 5·6; N, 3·6; S, 8·35. $C_{19}H_{23}O_6NS$ requires C, 58·0; H, 5·85; N, 3·55; S, 8·15%). With this compound was a contaminant, insoluble in dilute sodium carbonate solution, crystallising from aqueous ethanol as needles, m. p. 122° alone and with authentic N-3 : 4-*dimethoxybenzyltoluene*-p-*sulphonamide* (Found : C, 59·65; H, 5·9; N, 4·0. $C_{16}H_{19}O_4NS$ requires C, 59·8; H, 5·9; N, 4·3%).

Action of Polyphosphoric Acid on β-(3 : 4-*Dimethoxybenzylamino*)*propionic Acid*.—The acid (8 g.) in polyphosphoric acid (50 g.) was stirred and heated at 65—75° for 10 min. The red mixture was then diluted with ice and water, made alkaline with sodium carbonate, and extracted with chloroform. The residue, after removal of the solvent, formed a hydrochloride which crystallised from absolute ethanol in plates, m. p. 246—248° alone and mixed with 3 : 4-dimethoxybenzylamine hydrochloride (Found : C, 53·2; H, 6·9; Cl, 17·1. Calc. for $C_9H_{14}O_2NCl$: C, 53·1; H, 6·9; Cl, 17·4%).

Action of Polyphosphoric Acid on N-(3 : 4-*Dimethoxybenzyl*)-β-*toluene*-p-*sulphonamidopropionic Acid*.—The acid (100 mg.) was stirred at 18° with polyphosphoric acid (5 g.) for 10 min., becoming dark violet. The mixture was heated to 100° for 15 min., cooled, triturated with ice, and extracted with chloroform. The extract was dried and evaporated, and the residue crystallised from aqueous methanol in needles, m. p. 120—121° (25 mg.). The m. p. was raised to 121·5° on admixture with *N*-3 : 4-dimethoxybenzyltoluene-*p*-sulphonamide.

Ethyl γ-Bromobutyrate (cf. ref. 16).—A solution of butyrolactone (64·5 g.) in ethanol (250 ml.) was cooled to 0°, and a stream of dry hydrogen bromide was passed in (2 bubbles per second for 6 hr.). After 16 hr. at 0° the mixture was poured into cold water (1200 ml.). The oil which separated was removed; the aqueous layer was extracted with ethyl bromide (2 × 100 ml.) and the extracts were combined with the oil, washed with ice-cold 5% aqueous potassium hydroxide and water, and evaporated under reduced pressure. The residue distilled at 101—102°/26 mm. (135 g., 92%).

Ethyl γ-Toluene-p-*sulphonanilidobutyrate*.—*N*-Toluene-*p*-sulphonylaniline (49·4 g., m. p. 102°), ethyl γ-bromobutyrate (39 g.), anhydrous potassium carbonate (18 g.), and dry acetone (200 ml.) were refluxed for 22 hr. After cooling, the suspension was poured into cold water (1500 ml.) and extracted with chloroform, and the extract washed with aqueous sodium hydroxide and water, dried, and evaporated. The solid residue crystallised from light petroleum (b. p. 80—90°) in needles, m. p. 94—95° (62 g., 86%) (Found : C, 63·1; H, 6·25; N, 3·9. $C_{19}H_{23}O_4NS$ requires C, 63·15; H, 6·35; N, 3·9%). Starting material (3·4 g.) was recovered from the alkaline washings.

γ-Toluene-p-*sulphonanilidobutyric Acid*.—The above ester (7·25 g.) was dissolved in 1 : 4 v/v aqueous methanol (100 ml.) with slight warming, 10% aqueous potassium hydroxide (15 ml.) was added, and the mixture left for 16 hr. at 18—20°. The filtered solution was diluted with water (100 ml.), poured with stirring into an excess of dilute hydrochloric acid, and left for 1½ hr. The precipitate was collected, washed with water, dried, and crystallised from benzene in prisms, m. p. 165·5° (5·1 g., 76%). The yield on a 0·2-molar scale was *ca.* 100%

[14] Linstead and Meade, *J.*, 1934, 943.

(Found: C, 61·4; H, 5·6; N, 4·1; S, 9·45. $C_{17}H_{19}O_4NS$ requires C, 61·25; H, 5·7; N, 4·2; S, 9·6%).

Reactions of γ-Toluene-p-sulphonanilidobutyric Acid.—(1) *With polyphosphoric acid.* The acid (2·5 g.) was heated with polyphosphoric acid (30 g.) at 100° for 4 hr. with intermittent stirring and then poured on crushed ice. Chloroform-extraction afforded 1-phenyl-2-pyrrolidone which separated from light petroleum (b. p. 100—120°) in plates, m. p. 68—69° (0·5 g.) (Found: C, 74·25; H, 6·95; N, 9·0. Calc. for $C_{10}H_{11}ON$: C, 74·5; H, 6·9; N, 8·7%).

(2) *With thionyl chloride.* The acid (6 g.) was allowed to react with thionyl chloride (40 ml.) at room temperature for 15 min., then heated on the steam-bath for 15 min. and distilled. The product had b. p. 105—120°/0·05 mm. (6 g.) and on being boiled with aqueous sodium hydroxide for 5 min. deposited 1-phenyl-2-pyrrolidone. Vacuum-sublimation of the crude product (before distillation) gave toluene-*p*-sulphonyl chloride, m. p. and mixed m. p. 70°, whilst treatment of the distillate with aluminium chloride in benzene gave 1-phenyl-2-pyrrolidone and phenyl *p*-tolyl sulphone, m. p. and mixed m. p. 126°.

(3) The acid was recovered (95%) after treatment with hydrogen fluoride at 20° for 4 hr.

4-Toluene-p-sulphonamidoveratrole.—This *amide* was prepared in pyridine and crystallised from methanol in plates, m. p. 139° (Found: C, 58·45; H, 5·75; N, 4·5; S, 10·6. $C_{18}H_{17}O_4NS$ requires C, 58·65; H, 5·55; N, 4·55; S, 10·4%).

Ethyl γ-N-(3 : 4-Dimethoxyphenyl)toluene-p-sulphonamidobutyrate.—4-Toluene-*p*-sulphonamidoveratrole (61 g.), ethyl γ-bromobutyrate (39 g.), anhydrous potassium carbonate (40 g.), and dry acetone (120 ml.) were refluxed together for 15 hr., and worked up as before leaving a residue which distilled at 265—275°/0·04 mm. (75 g., 84%). After crystallisation from methanol this *ester* had m. p. 63° (Found: C, 60·0; H, 6·2; N, 3·35; S, 7·25. $C_{21}H_{27}O_6NS$ requires C, 59·8; H, 6·45; N, 3·3; S, 7·6%). Starting material (9 g.) was recovered from the alkaline washings.

The ester (75 g.) in methanol (400 ml.) was hydrolysed on a steam-bath for 40 min. with 15% aqueous sodium hydroxide (200 ml.). The product crystallised from aqueous ethanol as the *monohydrate*, prisms, m. p. 89° (68 g., 93%) (Found: C, 55·55; H, 6·25; N, 3·4; S, 8·1. $C_{19}H_{23}O_6NS,H_2O$ requires C, 55·45; H, 6·15; N, 3·4; S, 7·8%). The anhydrous *acid* was obtained by repeated crystallisation from ethyl acetate–light petroleum (b. p. 80—90°), forming needles, m. p. 127° (Found: C, 57·65; H, 5·75; N, 4·8; S, 8·1. $C_{19}H_{23}O_6NS$ requires C, 58·0; H, 5·9; N, 3·55; S, 8·15%).

1-[3 : 4-Dimethoxy-2(or 6)-toluene-p-sulphonylphenyl]-2-pyrrolidone.—The above anhydrous acid (1·3 g.) was heated at 100° for 1½ hr. with polyphosphoric acid (10 g.), cooled, diluted with water, and extracted with chloroform. The extract was washed with dilute aqueous sodium carbonate and water, dried, and evaporated. The residue crystallised from methanol in prisms, m. p. 198° (0·45 g., 36%) (Found: C, 60·7; H, 5·8; N, 3·8; S, 8·6. $C_{19}H_{21}O_5NS$ requires C, 60·75; H, 5·65; N, 3·75; S, 8·55%). The same *product* was obtained from the hydrated acid (m. p. 89°) at 50° but there was no reaction at 20°. It failed to form an oxime, semicarbazone, or 2 : 4-dinitrophenylhydrazone and could not be hydrogenated at room temperature and pressure in glacial acetic acid over a platinum catalyst.

Ethyl γ-[3 : 4-Dimethoxy-2(or 6)-toluene-p-sulphonanilido]butyrate.—Ethyl *γ-N-(3 : 4-dimethoxyphenyl)toluene-p-sulphonamidobutyrate* (2 g.) was heated with polyphosphoric acid (25 g.) for 10 min. at 95—100° with stirring. The dark mixture was cooled, diluted with water, and extracted with chloroform. The extract was washed with dilute aqueous sodium hydroxide, dilute hydrochloric acid, and water, dried, and evaporated. The *product* crystallised from light petroleum (b. p. 100—120°) (charcoal) in prisms, m. p. 127° (0·95 g., 48%) (Found: C, 60·2; H, 6·5; N, 3·3; S, 7·45. $C_{21}H_{27}O_6NS$ requires C, 59·8; H, 6·45; H, 3·3; S, 7·6%). Its infrared spectrum (in $CHCl_3$) showed bands at 1729 (ester C:O) and 3406 cm.$^{-1}$ (NH). It failed to form an oxime or a 2 : 4-dinitrophenylhydrazone.

This ester (0·4 g.) was refluxed for 1 hr. with 8% aqueous sodium hydroxide (20 ml.) and alcohol (5 ml.). The solution was cooled, filtered, and acidified to pH 5 and the *acid* extracted with chloroform. This crystallised from aqueous methanol as prisms, m. p. 173° (0·3 g., 80%) (Found: C, 57·65; H, 6·05; N, 3·6; S, 8·35. $C_{19}H_{23}O_6NS$ requires C, 58·0; H, 5·9; N, 3·55; S, 8·15%).

γ-N-(3 : 4-Dimethoxyphenyl)toluene-p-sulphonamidobutyric acid (0·5 g.) was heated with anhydrous stannic chloride (1·8 ml.) at 120° for 2 hr., cooled, treated with ice and concentrated hydrochloric acid, warmed on the steam-bath, and extracted, after cooling, with benzene and

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chloroform. The combined organic extracts were dried and evaporated, and the residual acid crystallised from benzene, and then from methanol, in prisms, m. p. 169—171°, raised to 172—173° on admixture with material prepared as above.

1-(3 : 4-*Dimethoxyphenyl*)-2-*pyrrolidone*.—(*a*) γ-*N*-(3 : 4-Dimethoxyphenyl)toluene-*p*-sulphonamidobutyric acid (5 g.) was stirred for 7 hr. with phosphoric oxide (10 g.), kieselguhr (5 g.), and sodium-dried benzene (100 ml.) under reflux. After the solvent had been evaporated, the residue was made alkaline with 30% aqueous sodium carbonate and extracted with ether. The extract was dried and evaporated, leaving a residue which distilled at 200—220°/0·04 mm. The distillate of *pyrrolidone* was repeatedly crystallised from light petroleum (b. p. 80—90°), to give needles, m. p. 83—84° (1 g.) (Found : C, 65·35; H, 6·8; N, 6·3. $C_{12}H_{15}O_3N$ requires C, 65·15; H, 6·85; N, 6·35%).

(*b*) The same acid (2 g.) was dissolved in anhydrous hydrogen fluoride (25 ml.), and the orange solution left at 20° for 24 hr. After treatment with excess of aqueous sodium carbonate the pyrrolidone was extracted with chloroform, distilled *in vacuo*, and crystallised from light petroleum in needles, m. p. 82°.

(*c*) The same acid (3 g.) was refluxed with thionyl chloride (25 ml.) for 10 min., then evaporated to dryness in a vacuum. When the residue was heated *in vacuo* a sublimate appeared which crystallised from light petroleum (b. p. 50—60°) in needles, m. p. 70°, undepressed on admixture with toluene-*p*-sulphonyl chloride. The material which failed to sublime was distilled at 220°/0·05 mm. and crystallised from light petroleum in needles, m. p. 82°, raised to 83° when mixed with the pyrrolidone prepared as in (*a*).

β-N-(3 : 4-*Dimethoxyphenyl*)*toluene*-p-*sulphonamidopropionic Acid*.—(*a*) Solutions of 4-toluene-*p*-sulphonamidoveratrole (20 g.) in 8% aqueous sodium hydroxide (33 ml.) and of β-chloropropionic acid (7·1 g.) in the same alkali (33 ml.) were mixed and refluxed for 16 hr. The mixture was then stirred in ice for 45 min., next filtered, and the residue washed with 5% aqueous sodium hydrogen carbonate. In this way starting material (12 g.; m. p. 139°) was recovered. The filtrate and washings were acidified, kept at 0° for 2 hr. with stirring, and filtered. The finely ground precipitate of *acid* was washed with cold water, dried, and crystallised from benzene in prisms, m. p. 130° (8 g., 81% based on sulphonamide consumed) (Found : C, 56·85; H, 5·75; N, 3·7; S, 8·4. $C_{18}H_{21}O_6NS$ requires C, 57·0; H, 5·6; N, 3·7; S, 8·45%).

(*b*) Propiolactone (0·75 ml.) was added dropwise to a stirred solution of 4-toluene-*p*-sulphonamidoveratrole (3·1 g.) in water (20 ml.) and 10% aqueous sodium hydroxide (4 ml.). Stirring was continued for 2 hr. and the solution then left overnight at 18°. The precipitate was collected and the alkaline filtrate acidified and extracted with chloroform. The extract was washed with aqueous sodium hydrogen carbonate which was then acidified and extracted, to yield a white solid which separated from benzene in prisms, m. p. 130° (0·1 g.). Starting material recovered from the original precipitate and chloroform solution amounted to 2·7 g.

1 : 2 : 3 : 4-*Tetrahydro*-6 : 7-*dimethoxy*-1-*toluene*-p-*sulphonyl*-4-*quinolone*.—The above acid (4·5 g.), phosphorus pentachloride (2·5 g.), and sodium-dried benzene (300 ml.) were refluxed for ½ hr. and cooled in ice. An ice-cold solution of anhydrous stannic chloride (3·5 ml.) in benzene (15 ml.) was added and the mixture was allowed to warm to 18° during 2½ hr. To the suspension was added ice, concentrated hydrochloric acid, and ether (15 ml.) : after 1 hr., the mixture was shaken, and the organic layer removed, washed with water, aqueous sodium hydroxide, and water, dried, and evaporated. The residual *quinolone* crystallised from methanol in prisms, m. p. 176·5° (2·5 g.) (Found : C, 60·05; H, 5·6; N, 4·1. $C_{18}H_{19}O_3NS$ requires C, 59·8; H, 5·3; N, 3·9%). The 2 : 4-*dinitrophenylhydrazone* was obtained from xylene as dark red needles, m. p. 240° (Found : C, 53·4; H, 4·45; N, 12·5. $C_{24}H_{23}O_6N_5S$ requires C, 53·2; H, 4·3; N, 12·95%).

1 : 2 : 3 : 4-*Tetrahydro*-6 : 7-*dimethoxy*-1-*toluene*-p-*sulphonylquinoline*.—The above quinolone (0·5 g.), hydrazine hydrate (0·25 ml., 90%), potassium hydroxide (0·25 g.), and diethylene glycol (5 ml.) were heated to 120° under reflux for 40 min., and the condenser was removed and dried while the reaction mixture was heated to 195—200°. The condenser was placed and the temperature kept at 200° for 1 hr., after which the mixture was cooled, poured into water, and left overnight. The *product* was collected and crystallised from methanol in prisms, m. p. 169° (50 mg.) (Found : C, 62·1; H, 6·1; N, 4·05; S, 9·1. $C_{18}H_{21}O_4NS$ requires C, 62·25; H, 6·1; N, 4·05; S, 9·25%).

β-[3 : 4-*Dimethoxy*-2(or 6)-*toluene*-p-*sulphonanilido*]*propionic Acid*.—β-*N*-(3 : 4-Dimethoxyphenyl)toluene-*p*-sulphonamidopropionic acid (1 g.) and polyphosphoric acid (10 g.) were

heated together (½ hr.) at 85°, left at 18° for 16 hr., then diluted with water, and the product was extracted with chloroform. It formed crystals, m. p. 191·5° (250 mg.) (from aqueous methanol). The *compound* was readily soluble in aqueous sodium carbonate (Found: C, 56·8; H, 5·6; N, 3·85. $C_{18}H_{21}O_6NS$ requires C, 57·0; H, 5·9; N, 3·7%).

N-*Toluene*-p-*sulphonphenethylamide*.—This *amide* crystallised from light petroleum (b. p. 80—90°) in needles, m. p. 66° (26·5 g., 97%) (Found: N, 5·35; S, 11·45. $C_{15}H_{17}O_2NS$ requires N, 5·1; S, 11·65%).

N-*Phenethyl*-N-*toluene*-p-*sulphonylglycine*.—The above sulphonamide (13·75 g.), ethyl chloroacetate (6·2 g.), anhydrous potassium carbonate (13 g.), and dry acetone (150 ml.) were refluxed together (24 hr.), cooled, poured into water, and extracted with chloroform. The residual oil was refluxed with aqueous sodium hydroxide (125 ml., 10%), and methylated spirit (125 ml.) for 1 hr. to give the *acid* which crystallised from ethyl acetate–light petroleum (b. p. 80—90°) in needles, m. p. 148—149° (7 g., 42%) (Found: C, 61·6; H, 5·7; N, 3·9; S, 9·25. $C_{17}H_{19}O_4NS$ requires C, 61·3; H, 5·7; N, 4·2; S, 9·6%). Some starting material was recovered from the sodium hydroxide washings.

1 : 2 : 3 : 4-*Tetrahydro*-2-*toluene*-p-*sulphonyl*isoquinoline.—(*a*) Toluene-*p*-sulphonyl chloride and tetrahydro*iso*quinoline were heated together in dry pyridine. The *sulphonamide* crystallised from methanol in needles, m. p. 145° (Found: C, 67·2; H, 5·9; N, 4·65. $C_{16}H_{17}O_2NS$ C, 66·9; H, 5·9; N, 4·9%).

(*b*) The preceding amino-acid (1 g.) was heated with polyphosphoric acid (10 g.) at 100° for 7½ hr., cooled, and diluted with water. The chloroform extract of this mixture was washed with aqueous sodium carbonate and water, dried, and evaporated. The residue crystallised from methanol as needles, m. p. 143° (0·5 g., 59%), raised to 144° on admixture with the preceding *iso*quinoline derivative.

5-*Toluene*-p-*sulphonyl*-5-*azabenzo*cyclo*hepten*-3-*one*.—*N*-Phenethyl-*N*-toluene-*p*-sulphonylglycine (2·5 g.) was refluxed with thionyl chloride (12 ml.) for 20 min. After removal of excess of thionyl chloride under reduced pressure, the residue was dissolved in dry carbon disulphide (50 ml.) and cooled in ice and concentrated hydrochloric acid. Anhydrous aluminium chloride (2 g.) was added with swirling and the suspension was left at 0° for 2 hr. with occasional agitation; after a further 2 hr. at 18°, the solvent was removed, ice-water added and the suspension left for 12 hr., then extracted with chloroform. The extract was washed with aqueous sodium carbonate, and water, dried, and evaporated. The residue crystallised from methanol or light petroleum (b. p. 100—120°) in needles, m. p. 121° (0·6 g.). Analysis indicated that this product was a mixture of the desired azabenzo*cyclo*heptenone and the *iso*quinoline already described, and the infrared spectrum showed only a weak band at 1684 $cm.^{-1}$ (Ar·C:O). It formed a 2 : 4-*dinitrophenylhydrazone* which separated from glacial acetic acid–methanol as orange crystals, m. p. 213° (Found: C, 55·5; H, 4·4; N, 14·4. $C_{23}H_{21}O_6N_5S$ requires C, 55·75; H, 4·25; N, 14·15%).

3 : 4-*Dimethoxy*-N-*toluene*-p-*sulphonphenethylamide*.—The *sulphonamide* crystallised from methanol in needles, m. p. 136° (13·5 g.) (Found: C, 60·75; H, 6·05; N, 3·9. $C_{17}H_{21}O_4NS$ requires C, 60·9; H, 6·3; N, 4·2%), insoluble in aqueous sodium hydroxide.

N-3 : 4-*Dimethoxyphenethyl*-N-*toluene*-p-*sulphonylglycine*.—The above sulphonamide (10·1 g.), ethyl chloroacetate (3·25 ml.), anhydrous potassium carbonate (10 g.) and dry acetone (100 ml.) were refluxed for 24 hr. The crude product was hydrolysed by refluxing 8% aqueous sodium hydroxide (50 ml.) and alcohol (75 ml.) for 1½ hr. The *acid* crystallised from ethyl acetate–light petroleum (b. p. 80—90°) in needles, m. p. 145° (6·8 g., 58%) (Found: C, 58·05; H, 6·1; N, 3·4. $C_{19}H_{23}O_6NS$ requires C, 58·0; H, 5·9; N, 3·55%). Some of the starting sulphonamide was recovered from the chloroform extract. When this acid was heated with polyphosphoric acid at 80—90° a dark red colour appeared within 5 min.; the product isolated was insoluble in aqueous sodium hydroxide but failed to form a 2 : 4-dinitrophenylhydrazone; it could not be purified.

4-*Methoxy*-4′-*methyldiphenyl Sulphone*.—Anisole (0·7 g.) and toluene-*p*-sulphonic acid monohydrate (1·2 g.) (or equiv. amount of the anhydrous sodium salt) were heated in polyphosphoric acid (30 g.) for 3½ hr. at 95°. Dilution of the red mixture with ice-water precipitated the sulphone. It crystallised from aqueous methanol in needles, m. p. 103° (65%).

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THE UNIVERSITY, OLD ABERDEEN, SCOTLAND. [*Received, November 16th*, 1956.]

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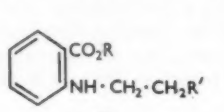
444. *Azabenzocycloheptenones. Part II.* Dieckmann Cyclisation of Arylamino-esters.*

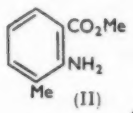
By G. R. Proctor and R. H. Thomson.

Attempted acyloin reduction of the diester (I; R = Me, R′ = CO_2Me) gave the quinolone (III; R = CO_2Me). Dieckmann cyclisation of the diester (IV; R = *p*-$C_6H_4Me{\cdot}SO_2$) yielded the azabenzo*cyclo*heptenone (V).

As the synthesis of azabenzo*cyclo*heptenones by Friedel–Crafts cyclisation is not practicable (see Part I *) alternative routes based on anthranilic acid derivatives have been explored. Cyanoethylation of anthranilic acid using acid catalysts [1] was unsuccessful but the nitrile (I; R = H, R′ = CN) was readily obtained in the presence of potassium hydroxide. Hydrolysis then gave the diacid (I; R = H, R′ = CO_2H) from which both the mono- (I; R = H; R′ = CO_2Me) and the di-methyl ester were obtained by the Fischer–Speier method. During attempts to obtain the diester directly from the nitrile (I; R = H; R′ = CN) it was found that prolonged reaction with methanolic sulphuric acid gave, in addition, a primary amine, regarded as (II) or a mixture of (II) and its isomer methyl 2-amino-5-methylbenzoate. This would arise by a β-elimination of acrylonitrile followed



(I)



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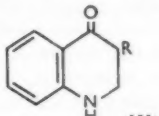

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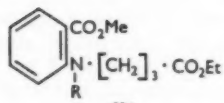

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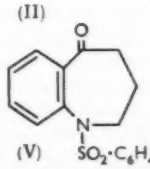

(V)

(or preceded) by *N*-methylation and $N \longrightarrow C$ migration of the methyl group. The original intention was to cyclise the diester (I; R = Me; R′ = CO_2Me) to an acyloin but in practice none of the seven-membered ring compound was obtained, the chief product being the keto-ester (III; R = CO_2Me) along with a little of the quinoline (III; R = H). A series of cyclic aza-acyloins has been made by Leonard and his co-workers [2] who found that cyclic aza-keto-esters were often formed at the same time and a seven-membered cyclic acyloin could only be obtained in 10% yield. We also prepared the quinoline (III; R = CO_2Me) under Dieckmann conditions but the yield was low, probably owing to the presence of a free NH group in the starting material. So we turned to the higher homologue (IV). The *N*-toluene-*p*-sulphonyl derivative (used to avoid lactam formation) was obtained by condensing methyl *N*-toluene-*p*-sulphonylanthranilate with ethyl γ-bromobutyrate, and when subjected to the Dieckmann reaction yielded, after hydrolysis, the azabenzo*cyclo*heptenone (V). The yield was again low and the crude product contained much starting material.

Experimental

N-2′-Cyanoethylanthranilic Acid.—Anthranilic acid (137 g.) was refluxed with acrylonitrile (53 g.), 40% aqueous potassium hydroxide (20 ml.), and ethanol (50 ml.) for 18 hr., then the solution was poured into cold water (2 l.), stirred, and adjusted to pH 5 with hydrochloric acid. The precipitated *acid* was collected and washed with cold water; it crystallised from ethanol (500 ml.)–water (400 ml.) in needles, m. p. 169° (127 g., 67%) (Found: C, 62·9; H, 5·35; N, 14·9. $C_{10}H_{10}O_2N_2$ requires C, 63·15; H, 5·3; N, 14·75%).

N-2′-Carboxyethylanthranilic Acid.—The above acid (40 g.) was refluxed with 20% aqueous

* Part I, preceding paper.

[1] Braunholz and Mann, *J.*, 1949, 67; 1952, 3046; 1953, 1817.
[2] Leonard, Fox, and Oki, *J. Amer. Chem. Soc.*, 1954, **76**, 5708.

potassium hydroxide (1 l.) until ammonia was no longer evolved. The cooled solution was filtered and neutralised with hydrochloric acid, and the precipitate collected and washed with cold water. The *diacid* crystallised from water in needles, m. p. 182° (95%) (Found : C, 57·65; H, 5·25; N, 7·0. $C_{16}H_{11}O_4N$ requires C, 57·4; H, 5·3; N, 6·7%). The *N-toluene-p-sulphonyl derivative* crystallised from aqueous methanol in needles, m. p. 188—189° (Found : C, 56·05; H, 4·6; N, 4·05; S, 8·75. $C_{17}H_{17}O_6NS$ requires C, 56·15; H, 4·7; N, 3·85; S, 8·8%). The *dimethyl ester* was obtained by refluxing the acid (46 g.) in dry methanol (500 ml.) while dry hydrogen chloride was passed into the solution. After 12 hr., the mixture was cooled to 0° and poured into a stirred 20% solution of sodium hydroxide (750 ml.) at <10°. After 15 hr. at 0°, the product was collected, washed with iced water, dried *in vacuo*, and crystallised from light petroleum (b. p. 40—60°), forming prisms, m. p. 36° (26·5 g.; 65% based on the acid consumed) (Found : C, 60·95; H, 6·35; N, 5·75. $C_{12}H_{15}O_4N$ requires C, 60·75; H, 6·35; N, 5·9%). Starting material (12 g.) was recovered. In one experiment when hydrogen chloride was passed for only 50 min., extraction of the neutral solution with chloroform gave a *monomethyl ester* which crystallised from light petroleum (b. p. 100—120°) in needles, m. p. 101° (Found : C, 59·15; H, 5·95; N, 6·25. $C_{11}H_{13}O_4N$ requires C, 59·2; H, 5·85; N, 6·3%) : it was soluble in cold sodium carbonate solution and gave a violet ferric chloride colour like the parent acid and nitrile (above). This is consistent with structure (I; R = H, R′ = CO_2Me) as the diester gave no colour. The diester gave a *monoester monoamide* which separated from light petroleum (b. p. 100—120°) in needles, m. p. 105° (Found : C, 59·2; H, 6·2; N, 12·7. $C_{11}H_{14}O_3N_2$ requires C, 59·45; H, 6·35; N, 12·6%).

Methyl 2-Amino-3-methylbenzoate.—*N*-2′-Cyanoethylanthranilic acid (230 g.) was heated on a steam-bath for 43 hr. with dry methanol (298 ml.) and concentrated sulphuric acid (136 ml.). The mixture was poured into cold water, made alkaline with sodium carbonate, and extracted with chloroform. The dried extract was evaporated and the bulk of the residue distilled at 180—190°/10 mm. Redistillation gave the diester as principal fraction, b. p. 186°/10 mm., m. p. 36°. The remainder, which did not solidify, was fractionated through a 25 cm. column and collected at 83°/0·05 mm. (Found : C, 65·6; H, 6·6; N, 9·1. Calc. for $C_9H_{11}O_2N$: C, 65·45; H, 6·65; N, 8·5%). Hydrolysis gave the amino-acid, m. p. 163·5° (from light petroleum, b. p. 100—120°) (Found : N, 9·45. Calc. for $C_8H_9O_2N$: N, 9·25%). The *hydrochloride* crystallised from anisole in needles, m. p. 175·5° (Found : Cl, 18·9. $C_8H_{10}O_2NCl$ requires Cl, 18·95%) (cf. lit., 2-amino-3-methylbenzoic acid, m. p. 168—169° [3] or 172° [4]; methyl ester, b. p. 153°/23 mm.[3]: 2-amino-5-methylbenzoic acid, m. p. 172° [5], 175° [4], or 177° [6]; methyl ester, m. p. 62°). The amino-ester (b. p. 83°/0·05 mm.) was diazotised and coupled with β-naphthol, giving an *azo-derivative* which separated from acetic acid or ethanol in red needles, m. p. 179° (Found : N, 9·05. $C_{18}H_{14}O_3N_2$ requires N, 9·15%).

1 : 2 : 3 : 4-*Tetrahydro-3-methoxycarbonyl-4-quinolone.*—(*a*) Methyl *N*-2′-methoxycarbonylethylanthranilate (9·25 g.) was refluxed for 22 hr. in sodium-dried benzene (75 ml.) containing finely dispersed sodium (1·2 g.) and ethanol (0·5 ml.). The mixture was then cooled, shaken with ice, and neutralised with hydrochloric acid. The benzene layer was separated and the aqueous layer extracted with chloroform. The combined organic solutions were dried and evaporated, and the *product* sublimed *in vacuo*. The sublimate separated from light petroleum (b. p. 100—120°) in yellowish-green crystals, m. p. 113° (0·47 g.) (Found : C, 64·4; H, 5·25; N, 6·6. $C_{11}H_{11}O_3N$ requires C, 64·4; H, 5·35; N, 6·85%). The **2 : 4-***dinitrophenylhydrazone* crystallised from ethyl acetate–light petroleum (b. p. 80—90°) in dark red needles, m. p. 221° (Found : C, 52·9; H, 4·2. $C_{17}H_{15}O_6N_5$ requires C, 53·0; H, 3·9%). The ON-*ditoluene-p-sulphonyl derivative* was prepared in pyridine, and crystallised from ethanol in needles, m. p. 136—137° (Found : C, 58·3; H, 3·95; N, 2·5; S, 11·95. $C_{35}H_{33}O_7NS_2$ requires C, 58·45; H, 4·5; N, 2·7; S, 12·45%). The residue after sublimation was a yellow oil which gave a 2 : 4-dinitrophenylhydrazone, m. p. 260° (from glacial acetic acid), not depressed on admixture with the 2 : 4-dinitrophenylhydrazone of 1 : 2 : 3 : 4-tetrahydro-4-quinolone.[7] Hydrochloric acid hydrolysis of the keto-ester, m. p. 113°, also gave a yellow oil which formed a 2 : 4-dinitrophenylhydrazone, m. p. and mixed m. p. 260° (Found : C, 54·9; H, 4·0; N, 21·0. Calc. for $C_{15}H_{13}O_4N_5$: C, 55·05; H, 4·0; N, 21·4%).

[3] Freundler, *Bull. Soc. chim. France*, 1907, **1**, 222.
[4] Findeklee, *Ber.*, 1905, **38**, 3553.
[5] Panaotović, *J. prakt. Chem.*, 1886, **33**, 63, 69.
[6] Anschütz and Schultz, *Ber.*, 1925, **58**, 65.
[7] Johnson, Woroch, and Buell, *J. Amer. Chem. Soc.*, 1949, **71**, 1903.

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(*b*) Methyl *N*-2′-methoxycarbonylethylanthranilate (10 g.) was dissolved in sodium-dried xylene (400 ml.) and added from a capillary to a suspension of finely divided sodium (5 g.) in boiling sodium-dried xylene (200 ml.) vigorously stirred under oxygen-free nitrogen in a creased * flask. Stirring was continued for ½ hr. after the addition was complete (8½ hr.), and after cooling, glacial acetic acid (15 g.) was added, followed by water (200 ml.), The mixture was made alkaline (pH 10) with sodium carbonate, the xylene layer was removed, and the aqueous layer was extracted with chloroform. The combined organic solutions were dried and evaporated, leaving an oil which distilled at 145°/0·05 mm. (0·5 g.). It was identified as the parent quinolone by its 2 : 4-dinitrophenylhydrazone, m. p. 260°. The solid residue was sublimed at 160°/0·05 mm. (4·2 g., 48%). Crystallised from light petroleum (b. p. 100—120°) it had m. p. 113°, undepressed on admixture with material prepared as in (*a*).

Methyl N-*Toluene*-p-*sulphonylanthranilate*.—Methyl anthranilate (50 g.) was treated with toluene-*p*-sulphonyl chloride (80 g.) in dry pyridine (160 ml.) and the product crystallised from methanol in prisms, m. p. 113° (92 g., 91%).

Ethyl γ-N-(2-*Methoxycarbonylphenyl*)-N-*toluene*-p-*sulphonamidobutyrate*.—The preceding ester (75 g.), ethyl γ-bromobutyrate (48 g.), anhydrous potassium carbonate (90 g.), and dry acetone (200 ml.) were refluxed together for 24 hr., cooled, poured into water (1 l.), and left for several hr., with stirring and cooling. The precipitate was filtered off, dried at 50°, and crystallised from ethyl acetate–light petroleum (b. p. 80—90°) in needles, m. p. 102—103° (89 g., 86%) (Found: C, 60·2; H, 5·9; N, 3·35; S, 7·15. $C_{21}H_{25}O_6NS$ requires C, **60·1**; H, 6·0; N, 3·35; S, 7·65%). Hydrolysis of the *ester* with aqueous 2N-sodium hydroxide gave a *diacid* which separated from aqueous ethanol in needles, m. p. 229—231° (Found: C, 57·4; H, 4·8; N, 4·0. $C_{18}H_{19}O_6NS$ requires C, 57·3; H, 5·05; N, 3·7%).

3-*Toluene*-p-*sulphonyl*-3-*azabenzo*cyclo*hepten*-7-*one*.—Potassium (2 g.) was dispersed in boiling sodium-dried benzene (200 ml.) stirred in a creased flask with a mechanical paddle and a nitrogen inlet. Dry oxygen-free nitrogen was passed into the flask while *tert.*-butyl alcohol (5·5 ml.) was cautiously added and washed into the solution with dry benzene. To this stirred, refluxing solution, a solution of the preceding diester (20 g.) in benzene (200 ml.) was added during 2 hr., an atmosphere of nitrogen being maintained. After being stirred and refluxed for 20 hr., the mixture was cooled and neutralised with dilute hydrochloric acid. The benzene layer was dried and evaporated, leaving a residue (18 g.) which contained starting material. (In one experiment 11 g. of the original ester were obtained by repeated crystallisation.) This residue was refluxed with alcohol (90 ml.) and concentrated hydrochloric acid (50 ml.) for 1½ hr., cooled, diluted with water (600 ml.), and extracted with chloroform. The extract was dried and evaporated, leaving an oil which gave a positive test with Brady's reagent. It was purified either by refluxing it with aqueous sodium hydroxide for ½ hr. or *via* its 2 : 4-dinitrophenylhydrazone. Pure ketone was obtained from the latter by the following modification of Rupe and Gassmann's procedure.[§] The 2 : 4-dinitrophenylhydrazone (4 g.), *m*-nitrobenzaldehyde (1·22 g.), *n*-butyl alcohol (100 ml.), and concentrated hydrochloric acid (2·0 ml.) were refluxed gently for 40 hr. and cooled to 10°. The mixture was filtered and the residue washed with methanol. The combined filtrate and washings were evaporated in a vacuum, leaving a product which crystallised from light petroleum (b. p. 100—120°) in needles, m. p. 126°, alone or mixed with the *ketone* obtained by alkaline hydrolysis (1·82 g.) (Found: C, 64·5; H, 5·6; N, 4·05. $C_{17}H_{17}O_3NS$ requires C, 64·7; H, 5·45; N, 4·45%). The infrared spectrum shows $\lambda_{C=O}$ 1688 cm.$^{-1}$ in CCl_4. Variation of the Dieckmann conditions failed to improve the yield. The 2 : 4-*dinitrophenylhydrazone* crystallised from acetic acid–ethanol or nitrobenzene as yellow needles, m. p. 236°. It was identical with the material obtained from the crude reaction product (Found: C, 55·7; H, 4·35; N, 14·2. $C_{23}H_{21}O_6N_5S$ requires C, 55·75; H, 4·25; N, 14·15%). The p-*nitrobenzylidene derivative* crystallised from glacial acetic acid in needles, m. p. 249—250° (Found: C, 63·95; H, 4·7; N, 5·95; S, 7·1. $C_{24}H_{20}O_5N_2S$ requires C, 64·25; H, 4·5; N, 6·25; S, 7·15%).

We thank Dr. V. C. Farmer for the infrared data, and Miss D. A. Thomson and Dr. R. A. Chalmers for some of the microanalyses.

THE UNIVERSITY, OLD ABERDEEN, SCOTLAND. [*Received, November* 16*th*, 1956.]

* *I.e.*, a flask in which indentations were made whilst hot.

§ Rupe and Gassmann, *Helv. Chim. Acta*, 1936, **19**, 569.

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445. *Aminoalkyl Tertiary Carbinols and Derived Products. Part V.* Antihistamines. The Stereochemistry of* cis- *and* trans-3-*Phenyl*-3-*pyridylallylamines.*

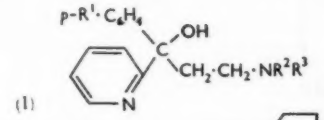
By D. W. Adamson, P. A. Barrett, J. W. Billinghurst, and T. S. G. Jones.

The allylamines prepared by sulphuric acid dehydration [1] of substituted 3-amino-1-phenyl-1-2′-pyridylpropan-1-ols have now been shown to be mixtures, separable by fractional crystallisation and base-exchange chromatography into pairs of isomers. Evidence, based partly on chemical reactions and partly on ultraviolet absorption spectra, is presented for the formulation of these pairs as *cis-trans*-isomers. The spectra indicate that the conjugated systems are different in the two isomers, the isomer designated *trans* having a spectrum similar to that of 2-vinylpyridine, and the spectrum of the isomer designated *cis* resembling that of styrene; these spectra are interpreted in terms of the co-planarity of one of the aryl groups with the ethylenic bond.

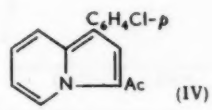
The conditions which determine the proportions in which the isomers are formed in the dehydration reaction have been investigated.

The synthesis of some 3-(tertiary amino)-1-aryl-1-2′-pyridylpropan-1-ols (I) and their dehydration by sulphuric acid to the corresponding allylamines, *e.g.*, (II), were described in Part III.[1] One of these allylamines (" 405C49 ") (II) was of especial interest for its very high antihistamine potency.[2,3]

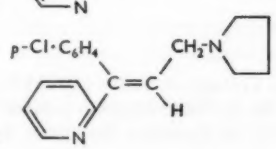
As reported briefly,[4] it has been found that, in addition to " 405C49," another base is present under certain conditions. The new base is isomeric with " 405C49 " and is relatively inactive pharmacologically. It is now shown that the bases are geometrical isomers, " 405C49 " being *trans* (II) and the other being *cis* (III) in terms of the relative positions of the nitrogen-containing groups.



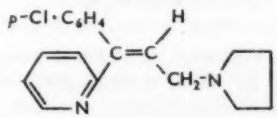
(I)



(IV)



(II)



(III)

The proportion of *trans*-isomer in the mixed allylamines is low when dehydration is carried out at room temperature, and increases with time and temperature of reaction and with increasing strength of sulphuric acid so that above a range of limiting conditions, defined in the Experimental section, it is the sole product of dehydration. The same conditions also quantitatively convert the *cis*- into the *trans*-isomers. Isomerisation is not, however, brought about by heat alone. On attempted distillation, a little *cis*-isomer distilled unchanged, but the bulk suffered gross decomposition.

Both isomers are oxidised by chromic acid in almost theoretical yield to 2-*p*-chlorobenzoylpyridine (identical with a specimen synthesised from 2-pyridyl-lithium and

* Part IV, *J.*, 1951, 52.

[1] Adamson and Billinghurst, *J.*, 1950, 1039.
[2] Bain, *Analyst*, 1951, **76**, 573.
[3] Green, *Brit. J. Pharmacol.*, 1953, **8**, 171.
[4] Adamson, Barrett, Billinghurst, Green, and Jones, *Nature*, 1951, **168**, 204.

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p-chlorophenyl cyanide); potassium permanganate gave a lower yield of the ketone. Both isomers gave the same propylamine [1] in high yield when hydrogenated in the presence of palladised charcoal. These reactions are consistent with formulation of the compounds as *cis-trans*-isomers. Some evidence for the particular configurations of the isomers was furnished by the study of their reaction with acetic anhydride. The *trans*-isomer was recovered substantially unchanged after 30 minutes' boiling, whereas the *cis*-isomer was completely degraded, one of the products being the pyrrocoline derivative (IV), whose constitution was confirmed by identity with material prepared from 2-4'-chlorobenzylpyridine by acetic anhydride which, following Chichibabin's interpretation [5] of the reaction first studied by Scholtz,[6] will have the unequivocal structure (IV). This ring-closure supports the configuration assigned to the *cis*-isomer.

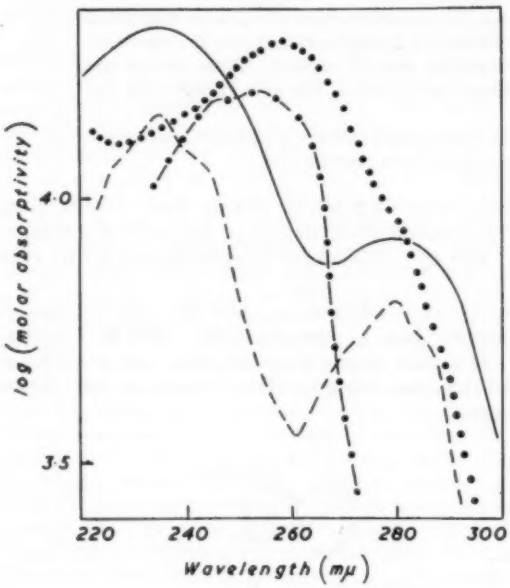


FIG. 1.

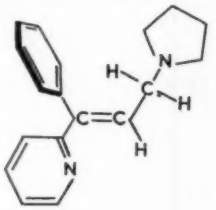
—— trans-1-p-*Chlorophenyl*-1-2'-*pyridyl*-3-*pyrrolidinoprop*-1-*ene* (*in* EtOH).
– – – 2-*Vinylpyridine* (*in* EtOH).
. . . cis-1-p-*Chlorophenyl*-1-2'-*pyridyl*-3-*pyrrolidinoprop*-1-*ene hydrobromide* (*in* H_2O).
·—· p-*Chlorostyrene* (*in* EtOH).

Professor R. Pepinsky, of Pennsylvania State College, recently provided final proof of the *cis*-structure by *X*-ray crystallographic studies of the analogous *p*-bromophenyl compound (personal communication); we are grateful to Professor Pepinsky for his interest in the problem.

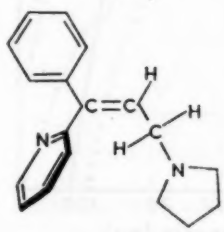
It is well known [7] that differences exist between the ultraviolet absorption spectra of some *cis*- and *trans*-isomers. The spectra are however usually similar in general character, there being only small differences in wavelength although the intensities may differ greatly. In contrast, the ultraviolet absorption spectra of the present isomers are highly distinctive.[4] The spectrum exhibited by the *trans*-isomer base in ethanol is very similar to that of 2-vinylpyridine in showing maximum absorption at 235 and 281 mμ (Fig. 1) while the *cis*-isomer has absorption bands closely resembling those of *p*-chlorostyrene in wavelength and intensity. These spectra may be interpreted in terms of the blocking effect of the component groups and of their relative spatial position about the double bond. It is impossible for a phenyl and a pyridyl ring joined to the same carbon atom to occupy

[5] Chichibabin and Stepanow, *Ber.*, 1929, **62**, 1068.
[6] Scholtz, *Ber.*, 1912, **45**, 734.
[7] Crombie, *Quart. Rev.*, 1952, **6**, 113.

the same plane, and the presence of the aminomethylene group on the β-carbon of the ethylene group must cause further steric hindrance. The hydrogen atoms of the methylene group are the cause of this hindrance, the tertiary nitrogen atom playing no part. It has long been postulated that for maximum conjugation in this type of structure co-planarity of the phenyl or of the pyridyl ring with the ethylene group is necessary. In view of the repulsive energy of the hindering hydrogen atoms, something less than complete overlap of the *p*-orbitals of each ring and the ethylene group will suffice. Recent studies [8] on derivatives of diphenyl have indicated that in this series large departures from co-planarity may be accommodated without loss of conjugation and of characteristic ultraviolet absorption. Nevertheless we believe that the ring more nearly occupying the plane of the ethylene group will be the more conjugated with the latter and we shall for brevity refer to these groups as co-planar. With this limitation in mind, it is possible to examine the detailed structures of the isomers in an attempt to interpret the spectra. The spectrum of the *trans*-isomer is so similar to that of 2-vinylpyridine that we deduce that the conjugated portions in the two molecules are also similar and that the pyridyl group and the ethylene group are nearly co-planar. The *p*-chlorophenyl group is then sufficiently inclined to the plane of the ethylene group to prevent conjugation with it and the contribution of the former to the near-ultraviolet absorption spectrum is small. Similarly[9] for the *cis*-isomer we deduce that the *p*-chlorophenyl group is the one in conjugation with the double bond. We therefore envisage the more detailed shapes of the molecules to be as illustrated diagrammatically in (V) and (VI).



(V)



(VI)

Since our preliminary communication,[4] Bauer and Lutz [9] have advanced a similar hypothesis to account for the difference in absorption spectra between some *cis*- and *trans*-dibenzoylstyrenes.

The ultraviolet absorption spectra of the isomers when determined in acid solution (Fig. 2) are also in accordance with the above hypothesis. In the first place the spectra of the *trans*-base and its monohydrochloride in water are indistinguishable. This is explicable if the nitrogen atom of the pyrrolidino-group does not interact with the double bond and is not itself hindered in salt formation by the rest of the molecule. The monohydrochloride must be formed exclusively through the pyrrolidino-group because of the great disparity in the strengths of the basic centres. In more strongly acid solution the peak at 281 mμ appears at progressively longer wavelengths and is increased in intensity. A similar difference is noted between the spectra of 2-vinylpyridine in neutral and in acid solution, presumably owing to an increase in the energy of the ground state of the salt relative to that of the excited state. In contrast, the spectrum of the *cis*-isomer in acid solution differs little from the styryl-like spectrum of the base, thereby confirming that the 2-pyridinium group of the salt, like the neutral 2-pyridyl group of the base, is not in conjugation with the double bond. It may be mentioned that the spectra of the isomers in acid

[8] Beavan, Hall, Lesslie, and Turner, *J.*, 1952, 854.
[9] Bauer and Lutz, *J. Amer. Chem. Soc.*, 1953, **75**, 5997.

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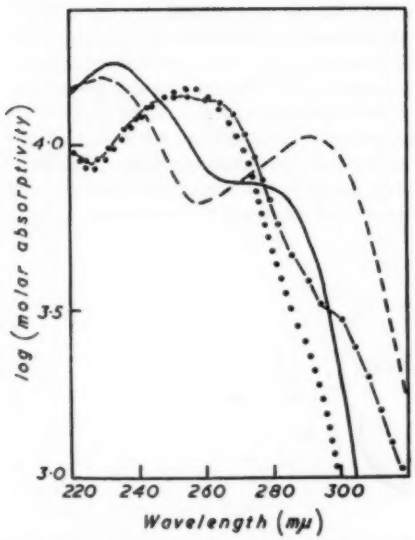
solution dispose of the remote possibility (considered in the earlier stages of the work and not rigorously excluded by the evidence from the oxidation) that the isomers differed in respect of the position of the double bond, one isomer having the vinylamine group, $-CH{:}CH{\cdot}N$, since it has been shown [10] that compounds containing this group show a great diminution in ultraviolet light absorption on conversion from base into cation.

The strength of the two basic centres of each isomer is of interest in relation to the structures proposed, and a detailed investigation will be reported elsewhere (Everett and Jones). Not unexpectedly, the strength of the pyrrolidino-groups in the two isomers is almost identical [for (V) pK_a' was $9{\cdot}46 \pm 0{\cdot}03$ and for (VI) $9{\cdot}51 \pm 0{\cdot}07$, at 25° and ionic

FIG. 2.



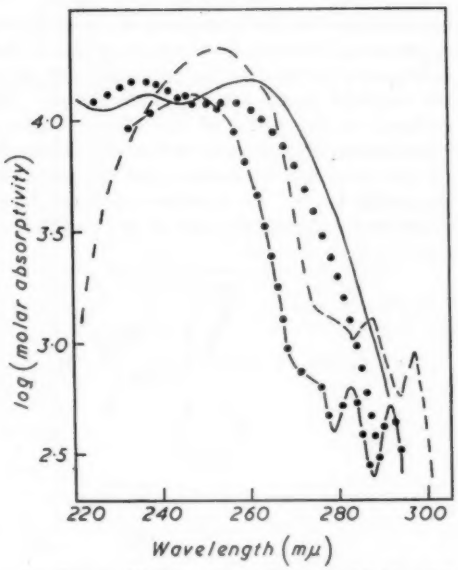
trans-1-p-*Chlorophenyl*-1-2′-*pyridyl*-3-*pyrrolidinoprop*-1-*ene*:

—— *in* 0·05M-*aq.* NaOH.
– – – *in* 1·0M-*aq.* HCl.

cis-1-p-*Chlorophenyl*-1-2′-*pyridyl*-3-*pyrrolidinoprop*-1-*ene*:

. . . *in* 0·1M-*aq.* NaOH.
·—· *in* 0·1M-*aq.* HCl.

FIG. 3.



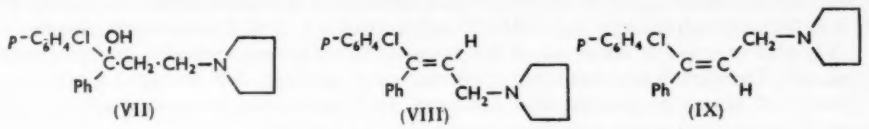
—— *Isomer* (VIII) *of* 1-p-*chlorophenyl*-1-*phenyl*-3-*pyrrolidinoprop*-1-*ene* (*in* EtOH)
– – – p-*Chlorostyrene* (*in* EtOH).
. . . *Isomer* (IX) *of* 1-p-*chlorophenyl*-1-*phenyl*-3-*pyrrolidinoprop*-1-*ene* (*in* EtOH).
·—· *Styrene* (*in hexane* [12]).

strength 0·05]. For the other (pyridyl) basic centres, the values found were: (V) 3·21 and (VI) 2·47 (at 25° and zero ionic strength). Reasons for this difference, and also for the unexpectedly low value, especially for (VI), will be advanced in the proposed publication.

The occurrence of geometrical isomerism has been observed also in the related series of diphenylallylamines in which the phenyl groups are dissimilarly substituted, and the spatial configuration of the isomers may be deduced from their spectra in the same way as in the pyridyl series. The phenomenon is thus general and not dependent on a feature peculiar to the 2-pyridyl group. Dehydration of the alcohol (VII) gave a mixture from which two pure, sharply defined allylamines, differing in their pharmacological activities, were isolated. The ultraviolet absorption spectra of the isomers, although similar, revealed

[12] Bowden, Braude, Jones, and Weedon, *J.*, 1946, 49.

differences in the wavelengths and intensity of their main absorption peaks of the same magnitude as the differences observed between *p*-chlorostyrene and styrene (Fig. 3). It is



therefore concluded that in one isomer the *p*-chlorophenyl group is co-planar with the double bond and *trans* to the aminomethylene group (VIII) while in the other, (IX), the unsubstituted phenyl group is *trans* to the aminomethylene group.

We have re-examined the dehydration of the other analogous alcohols (I; $R^1 = H$ or Cl; $NR^2R^3 = NMe_2$, NEt_2, $N<C_4H_8$, $N<C_5H_{10}$, $N<C_5H_8>O$) listed in Table 2 of

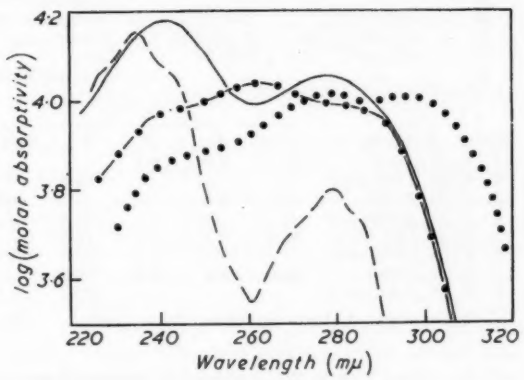
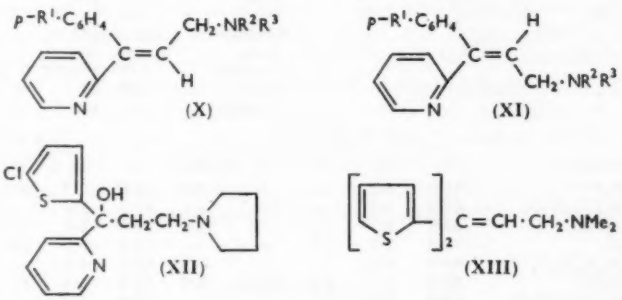


FIG. 4.

—— trans-1-2′-*Pyridyl*-1-(5-*chloro*-2-*thienyl*)-3-*pyrrolidinoprop*-1-*ene*.
– – – 2-*Vinylpyridine*.
. . . cis-1-2′-*Pyridyl*-1-(5-*chloro*-2-*thienyl*)-3-*pyrrolidinoprop*-1-*ene*.
·—· 1 : 1-*Di*-2′-*thienylprop*-1-*ene*.
All in EtOH.

Part III [1] and of some new *p*-substituted-phenylcarbinols (I; $R^1 = F$, Br, MeO; $NR^2R^3 = N < C_4H_8$) and a thienyl analogue (XII). The majority of the alcohols, when heated with 85—98% sulphuric acid at 100° for 10—30 min., gave mixtures of the allylamines



which were separated into *cis-trans*-isomers (X) and (XI). More dilute sulphuric acid was required in the cases of the more sensitive compounds (I; $R^1 = MeO$) and (XII). The more stable isomer (X) of each pair, like (II), exhibited the characteristic 2-vinylpyridine-like ultraviolet absorption and was the *trans*-isomer, and the other less stable isomer (XI), like (III), gave a spectrum similar to that of styrene or of the corresponding *para*-substituted styrene, and was the *cis*-isomer.

The isomeric allylamines derived from (XII) were of interest as examples in which

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neither of the chromophoric groups was phenyl. In conformity with the hypothesis one isomer (*trans*) showed the " orthodox " 2-vinylpyridine-like spectrum (Fig. 4), whereas the other (*cis*) exhibited a distinctive ultraviolet absorption spectrum similar to that of the 3 : 3-di-2′-thienylallylamines (*e.g.*, XIII),[11] and to that of 1 : 1-di-2′-thienylprop-1-ene.

A further example of isomerism of this type has recently been provided by Cymerman-Craig and Harrisson,[12] who separated the isomeric *cis*- and *trans*-3-(4-methyl-1-piperazino)-1-phenyl-1-2′-thienylprop-1-enes and compared their ultraviolet absorption spectra with those of known compounds possessing analogous chromophores.

TABLE 1. *Aryl 2-(tertiary amino)ethyl ketones*, $R^1{\cdot}CO{\cdot}CH_2{\cdot}CH_2{\cdot}NR^2R^3$.

No.	R^1	NR^2R^3	Compound	M. p.	Solvent for crystn.
1	*p*-C_6H_4F	$N<[CH_2]_4$	Base	55—56°	Pet †
2	"	"	Hydrochloride	153	EtOH–EtOAc
3	*p*-C_6H_4Br	$N<[CH_2]_4$	Base	79—80	EtOH
4	"	"	Hydrochloride	197—198	EtOH
5	*p*-$MeO{\cdot}C_6H_4$	$N<[CH_2]_4$	Hydrochloride	183—183·5	EtOH
6	2-(5-Cl-C_4H_2S)	$N<[CH_2]_4$ *	Hydrochloride	189 *	EtOH
7	*p*-C_6H_4Cl	NMeEt	Base	13—14	—
8	"	"	Hydrochloride	148·5—150	EtOH–EtOAc

		Found (%)					Required (%)				
No.	Formula	C	H	N	Cl	Br/F/S	C	H	N	Cl	Br/F/S
1	$C_{12}H_{16}ONF$	70·4	7·0	6·2	—	8·2	70·6	7·2	6·3	—	8·6
2	$C_{12}H_{16}ONF,HCl$	—	—	—	14·0	7·7	—	—	—	13·8	7·4
3	$C_{12}H_{16}ONBr$	55·6	5·6	—	—	28·6	55·3	5·7	—	—	28·4
4	$C_{12}H_{16}ONBr$	—	—	—	11·4	—	—	—	—	11·1	—
5	$C_{14}H_{19}O_3N,HCl$	62·3	7·5	5·2	13·5	—	62·3	7·4	5·2	13·2	—
6	$C_{11}H_{16}ONS,HCl$	—	—	5·3	25·5	11·4	—	—	5·0	25·4	11·4
7	$C_{12}H_{16}ONCl$	63·6	6·8	6·4	15·3	—	63·9	7·1	6·2	15·7	—
8	$C_{12}H_{16}ONCl,HCl$	—	—	—	27·2	—	—	—	—	27·1	—

* Decomp. † Light petroleum (b. p. <40°). * The reaction solvent was glacial acetic acid.

TABLE 2. *1-Aryl-1-2′-pyridyl-3-(tertiary amino)propan-1-ols*, $C_5H_4N{\cdot}CR^1(OH){\cdot}CH_2{\cdot}CH_2{\cdot}NR^2R^3$.

No.	R^1	NR^2R^3	Yield (%)	Compound	M. p.	Solvent for crystn.
1	*p*-C_6H_4F	$N<[CH_2]_4$	69	Base	91·5—93°	EtOH
2	"	"	—	Oxalate	154—155 *	MeOH–EtOH
3	*p*-C_6H_4Br	$N<[CH_2]_4$	72	Base	143·5—145	EtOH
4	*p*-$MeO{\cdot}C_6H_4$	$N<[CH_2]_4$	71	Base	82—83	EtOH
5	"	"	—	Oxalate	142·5—143 *	EtOH–EtOAc
6	2-(5-Cl-C_4H_2S)	$N<[CH_2]_4$	51	Base	90—90·5	EtOH
7	"	"	—	Oxalate	149—150·5 *	EtOH–EtOAc
8	*p*-C_6H_4Cl	NMeEt	—	Base	46—47	Pet †
9	"	"	—	Oxalate	160—162 *	MeOH

		Found (%)					Required (%)				
No.	Formula	C	H	N	Cl	Br/F/S	C	H	N	Cl	Br/F/S
1	$C_{18}H_{21}ON_2F$	71·9	6·8	9·5	—	6·5	72·0	7·0	9·3	—	6·3
2	$C_{18}H_{21}ON_2F,C_2H_2O_4$	61·3	5·7	—	—	5·1	61·5	5·9	—	—	4·9
3	$C_{18}H_{21}ON_2Br$	59·9	5·7	7·8	—	22·6	59·8	5·8	7·8	—	22·2
4	$C_{19}H_{24}O_3N_2$	73·2	7·7	9·0	—	—	73·1	7·7	9·0	—	—
5	$C_{19}H_{24}O_3N_2,C_2H_2O_4$	62·5	6·2	—	—	—	62·7	6·5	—	—	—
6	$C_{18}H_{19}ON_2ClS$	59·6	5·7	8·8	11·3	9·6	59·5	5·9	8·7	11·0	9·9
7	$C_{18}H_{19}ON_2ClS,C_2H_2O_4$	52·4	5·3	—	—	—	52·4	5·1	—	—	—
8	$C_{17}H_{21}ON_2Cl$	66·9	6·8	8·9	11·2	—	67·0	6·9	9·2	11·7	—
9	$C_{17}H_{21}ON_2Cl,\frac{1}{2}C_2H_2O_4$	61·4	6·0	—	—	—	61·8	6·3	—	—	—

*† See Table 1.

Dehydration of the alcohols (I; R^1 = halogen) under more severe conditions led, as in the example discussed in detail above, to the exclusive production of the *trans*-isomer

[11] Adamson, Part II, *J.*, 1950, 885.
[12] Cymerman-Craig and Harrisson, *Austral. J. Chem.*, 1955, **8**, 378.

(X; R^1 = halogen). The course of the dehydration of alcohols (I; R^1 = H or MeO) or (XII) was less clear-cut since the product was unstable to sulphuric acid at higher temperatures (*e.g.*, complete breakdown occurred rapidly at 200°). In these cases, use of lower temperatures was successful for the preparation of the pure *trans*-isomers, though in low yield. The *trans*- were more stable than the *cis*-isomers to the action of boiling acetic anhydride as in the case of (II) and (III), but again the difference in stability was more pronounced when the phenyl group was substituted by *p*-halogen than when it was unsubstituted.

We conclude from a re-examination of the allylamine salts described in Table 2 of Part III [1] that, despite their apparent homogeneity, with the exception of "405C49," they were mixtures of *cis-trans*-isomers in proportions which varied greatly, depending on the conditions of their formation and purification.

Fractional crystallisation of the neutral oxalates from ethanol generally separated the isomers (Table 3). Three bases were crystalline. This property apparently bears no simple relation to geometrical configuration, since two of the solids (X; R^1 = Cl and Br; $NR^2R^3 = N{<}C_4H_8$) were *trans* and one (XI; R^1 = Cl, $NR^2R^3 = NMe_2$) was the *cis*-isomer.

Chromatography on alumina gave only partial separation of two examples (Table 3, *g* and *l*).

Ion-exchange chromatography, which was not introduced until the later stages of the work, gave sharp separation with good recovery of the pure isomers.[13] The material selected was a sulphonated polystyrene resin (nominal cross-linking, 2·25%) in bead form, kindly supplied by the Chemical Research Laboratory, Teddington. The crude dehydration product was absorbed on the resin column and displaced with aqueous-alcoholic ammonia. The identity of the fractions and the point at which one isomer gave place to the other were established by ultraviolet spectroscopy.

The customary criteria of purity (*i.e.*, analysis, sharp m. p. unchanged on further crystallisation) are not adequate in all cases to make it certain that any given isomer has been obtained free from its partner. It is possible to be confident of the purity of the *trans*-isomers for several reasons, *viz.*: the relative insolubility of their oxalates in ethanol; the formation of identical material by different methods of separation and by treatment with acetic anhydride or concentrated sulphuric acid; and the specific nature of the absorption spectrum. The evidence for the purity of the *cis*-isomers is less clear. The absorption spectra are less characteristic and do not reveal contamination by a small proportion of the *trans*-isomer. On the other hand, the antihistamine potency of the *cis*-isomer is considerably lower (in some examples, nearly one hundred times) than that of the *trans*-isomer. It is concluded that in some cases physical evidence (*e.g.*, a crystalline base, or relatively insoluble salt) indicated a very high degree of purity, and in the others contamination by no more than a few per cent. of the *trans*-isomer is presumptive.

The compounds have been examined for their antihistamine and other biological effects by Mr. A. F. Green of the Pharmacology Laboratory. The relation between the structure of these and related compounds and their biological activities will be discussed elsewhere.

Experimental

M. p.s of salts are all with decomposition.

Dehydration of 1-p-*Chlorophenyl*-1-2′-*pyridyl*-3-*pyrrolidinopropan*-1-*ol* (Part III; [1] VI*g*).—The alcohol (20 g.) in concentrated sulphuric acid (100 ml.) was heated on the steam-bath for 15 min., cooled, poured on ice, and basified with aqueous ammonia, and the liberated oil was extracted into ether. Removal of the solvent by distillation gave a mixture of the isomeric allylamines (II = X*g* and III = XI*g*) as a pale brown oil (18 g., 95%).

[13] Jones, *Analyst*, 1952, **77**, 962; "Ion Exchange and Its Applications" (Report of Symposium), Soc. Chem. Ind., London, 1955, p. 164.

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Separation of the trans- *and* cis-*Isomers of* 1-p-*Chlorophenyl*-1-2′-*pyridyl*-3-*pyrrolidinoprop*-1-*ene* (Table 3; Xg and XIg).—(a) *By fractional crystallisation of oxalates* (Table 3, method A). The mixture of bases (18 g.) was dissolved in ethanol (50 ml.), and oxalic acid dihydrate (7·6 g., 1 mol.) in a little ethanol was added. The mixed oxalates rapidly crystallised and were collected, washed with ethanol and ether, and dried (21 g.; m. p. 148—155°). Numerous crystallisations from ethanol gave the *trans*-isomer oxalate (X*g*), needles, m. p. 184° (5·8 g., 23%) [Part III [1] (VII*g*) gives m. p. 177°]. The earlier filtrates were concentrated and allowed to crystallise, the crude *cis*-isomer oxalate separating as plates (m. p. 151—152°). It was freed from a little *trans*-isomer by crystallisation from chloroform to give prismatic needles, m. p. 156—157°, which, after drying in the air, contained 1 mol. of chloroform, lost on drying at 100° [Found: C, 49·7; H, 4·3; Cl, 24·6; loss at 100°, 22·4; Cl (after drying), 9·4. $C_{18}H_{19}N_2Cl,C_2H_2O_4,CHCl_3$ requires C, 49·6; H, 4·3; Cl, 27·9; loss, 23·6; Cl (after drying), 9·1%]. The chloroform was removed by crystallisation from ethanol, cis-1-p-*chlorophenyl*-1-2′-*pyridyl*-3-*pyrrolidinoprop*-1-*ene oxalate* (XI*g*) being obtained as plates (8·5 g., 34%), m. p. 156—157°.

The trans-*isomer base*, liberated from the oxalate by alkali, distilled without decomposition (b. p. 180—182°/0·2 mm.). It solidified and after crystallisation from light petroleum (b. p. 40—60°) formed prisms, m. p. 61—62°, n_D^{19} 1·603 (supercooled) (Found: C, 72·3; H, 6·3; N, 9·1; Cl, 11·4. $C_{18}H_{19}N_2Cl$ requires C, 72·4; H, 6·3; N, 9·4; Cl, 11·9%). Light absorption in 4×10^{-4}M-solution in EtOH: max. 235, 281 mμ (log ε 4·33, 3·93); in 4×10^{-5}M-solution in 5·5M-HCl: max. 227, 293 mμ (log ε 4·14, 4·00).

The cis-*isomer base* (5 g.), liberated from the oxalate, distilled without decomposition to give a colourless oil, b. p. 172—176°/0·1 mm., n_D^{19} 1·600 (Found: C, 72·4; H, 6·3; N, 9·2; Cl,

TABLE 3. 3-(*Tertiary amino*)-1-*aryl*-1-2′-*pyridylprop*-1-*ene isomers* (X *and* XI).

Compound [a]	R[1]	NR^2R^3	Separation [b]	Salt [c]	M. p. [d]	Mixed M. p. [d]	Peak ultraviolet light absorption [e] λ	log ε	λ	log ε
X*a*	H	NMe_2	A, D, E	Oxalate	179°	168—171°	238	4·32	280	4·03
XI*a*	,,	,,	A	,,	180—181		247	4·35	—	—
X*b*	H	NEt_2	A, B, D	,,	130—131	130—132	235	4·13	281	3·86
XI*b*	,,	,,	B	,,	163		252	4·10	—	—
X*c*	H	$N<[CH_2]_4$	B, D, E	,,	164—165	154—156	237	4·21	280	3·95
XI*c*	,,	,,	B	,,	169—170		251	4·18	—	—
X*d*	H	$N<[CH_2]_5$	A, D	,,	173—174	168—170	237	4·16	281	3·82
XI*d*	,,	,,	A	,,	175—176		256	4·30	—	—
X*e*	Cl	NMe_2	A, D, E	,,	182—183	167—169	237	4·44	280	4·11
XI*e*	,,	,,	A, F	,,	174—175		255	4·45	—	—
,,	,,	,,		Base [i]	61—62 *		—	—	—	—
X*f*	Cl	NEt_2	A, D	Oxalate [g]	130—131	120—125	235	4·26	281	3·88
XI*f*	,,	,,	A	,,	155—156		257	4·32	—	—
X*g*	Cl	$N<[CH_2]_4$	A, B, C,	Base [i]	61—62 *	—	235	4·33	281	3·93
,,	,,	,,	D, E, F	HCl [h]	180—182		234	4·34	273	4·01 ‡
,,	,,	,,		HBr [h]	183—184		229	4·40	273	4·04 ‡
,,	,,	,,		Oxalate	184	}	235	4·31	280	3·93
XI*g*	Cl	$N<[CH_2]_4$	A, C	HBr [h]	135—136	153—154	258	4·36	—	— ‡
,,	,,	,,		Oxalate [g]	157	}	258	4·33	—	— ‡
X*h*	Cl	$N<[CH_2]_5$	A, D, E	,,	175—176	162—165	234	4·26	280	3·91
XI*h*	,,	,,	A	,,	173—174		257	4·33	—	—
X*i*	Cl	$N<[CH_2]_4>O$	A, D	,,	187	160—161	236	4·29	281	3·94
XI*i*	,,	,,	A	,,	164—165		255	4·20	—	—
X*j*	Cl	NMeEt	D	,, [j]	161—162	148—150	235	4·25	280	3·86
XI*j*	,,	,,	A	,,	157		257	4·29	—	—
X*k*	F	$N<[CH_2]_4$	B	,, [f]	184—185	—	238	3·90	281	3·67
XI*k*	,,	,,	B	,,	166—167		252	3·90	280	3·67
X*l*	Br	$N<[CH_2]_4$	B, C, E,	Base [i]	90—91 *	—	238	4·28	280	3·86
,,	,,	,,	F	HCl [h]	179—180		232	4·28	265	3·89 ‡
,,	,,	,,		HBr [h]	186—188		235	4·30	280	3·90
,,	,,	,,		Oxalate [f]	182—183		—	—	—	—
XI*l*	,,	,,	B, C	HBr [h]	159—160	—	259	4·29	—	—
,,	,,	,,		Oxalate	163—164		259	4·30	—	—
X*m*	MeO	$N<[CH_2]_4$	B	Oxalate [f]	179—180	—	233	4·28	277	3·99
XI*m*			B	,,	140—142		237	4·18	270	4·13
X*n*	2-(5-Cl·C_4H_3S)[k]	$N<[CH_2]_4$	B, E	,, [f]	148—149	142—143	241	4·15	278	4·06
XI*n*			B	,,	155—156			(see Fig. 3)		

TABLE 3. (*Continued.*)

Compound	Formula	Found (%) C	H	N	Cl	Br/F/S	Required (%) C	H	N	Cl	Br/F/S
X*a*	$C_{16}H_{18}N_2,C_2H_2O_4$	65·8	6·0	8·6	—	—	65·8	6·1	8·5	—	—
XI*a*	,,	65·7	5·9	8·3	—	—	,,	,,	,,	—	—
X*b*	$C_{18}H_{22}N_2,C_2H_2O_4$	67·7	6·7	7·8	—	—	67·4	6·7	7·9	—	—
XI*b*	,,	67·6	6·8	7·9	—	—	,,	,,	,,	—	—
X*c*	$C_{18}H_{20}N_2,C_2H_2O_4$	67·7	6·1	8·1	—	—	67·8	6·2	7·9	—	—
XI*c*	,,	67·7	6·1	8·1	—	—	,,	,,	,,	—	—
X*d*	$C_{19}H_{22}N_2,C_2H_2O_4$	68·2	6·4	7·4	—	—	68·5	6·5	7·6	—	—
XI*d*	,,	68·3	6·4	7·5	—	—	,,	,,	,,	—	—
X*e*	$C_{16}H_{17}N_2Cl,C_2H_2O_4$	59·3	5·0	7·7	9·9	—	59·6	5·2	7·7	9·8	—
XI*e*	,,	59·8	5·1	8·1	10·0	—	,,	,,	,,	,,	—
,,	$C_{16}H_{17}N_2Cl$	70·4	6·2	10·3	13·1	—	70·4	6·3	10·3	13·0	—
X*f*	$C_{16}H_{21}N_2Cl,C_2H_2O_4$	61·6	5·7	7·2	—	—	61·4	5·9	7·2	9·1	—
XI*f*	,,	61·4	5·7	7·1	—	—	,,	,,	,,	,,	—
X*g*	$C_{18}H_{19}N_2Cl$	72·3	6·3	9·1	11·4	—	72·4	6·3	9·4	11·9	—
,,	$C_{18}H_{19}N_2Cl,HCl$	—	—	—	21·0	—	—	—	—	21·2	—
,,	$C_{18}H_{19}N_2Cl,HBr$	—	—	—	—	21·1	—	—	—	—	21·1
,,	$C_{18}H_{19}N_2Cl,C_2H_2O_4$	61·9	5·5	7·1	9·3	—	61·8	5·4	7·2	9·1	—
XI*g*	$C_{18}H_{19}N_2Cl,HBr$	—	—	—	—	20·8	—	—	—	—	21·1
,,	$C_{18}H_{19}N_2Cl,C_2H_2O_4$	61·5	5·2	7·1	9·2	—	61·8	5·4	7·2	9·1	—
X*h*	$C_{19}H_{21}N_2Cl,C_2H_2O_4$	63·0	5·7	6·7	8·7	—	62·6	5·7	7·0	8·8	—
XI*h*	$C_{19}H_{21}N_2Cl,C_2H_2O_4$	62·4	5·7	7·0	8·2	—	,,	,,	,,	,,	—
X*i*	$C_{18}H_{19}ON_2Cl,C_2H_2O_4$	59·5	5·3	7·1	8·7	—	59·3	5·2	6·9	8·8	—
XI*i*	,,	59·2	5·4	6·7	8·9	—	,,	,,	,,	,,	—
X*j*	$C_{17}H_{19}N_2Cl,C_2H_2O_4$	60·8	5·7	7·2	9·1	—	60·6	5·6	7·4	9·4	—
XI*j*	,,	61·1	5·9	7·1	9·0	—	,,	,,	,,	,,	—
X*k*	$C_{18}H_{19}N_2F,C_2H_2O_4$	64·6	5·5	7·7	—	4·7	64·5	5·6	7·5	—	5·1
XI*k*	,,	64·7	5·6	7·2	—	5·5	,,	,,	,,	—	,,
X*l*	$C_{18}H_{19}N_2Br$	63·0	5·4	7·9	—	23·2	63·0	5·5	8·2	—	23·3
,,	$C_{18}H_{19}N_2Br,HCl$	—	—	—	9·3	—	—	—	—	9·4	—
,,	$C_{18}H_{19}N_2Br,HBr$	—	—	—	—	37·6	—	—	—	—	37·7
,,	$C_{18}H_{19}N_2Br,C_2H_2O_4$	55·3	5·0	—	—	—	55·4	4·8	—	—	—
XI*l*	$C_{18}H_{19}N_2Br,HBr$	—	—	—	—	37·8	—	—	—	—	37·7
,,	$C_{18}H_{19}N_2Br,C_2H_2O_4$	55·3	4·7	—	—	—	55·4	4·8	—	—	—
X*m*	$C_{19}H_{22}ON_2,C_2H_2O_4$	65·5	6·1	7·4	—	—	65·6	6·3	7·3	—	—
XI*m*	,,	66·1	6·5	7·4	—	—	,,	,,	,,	—	—
X*n*	$C_{17}H_{17}N_2ClS,C_2H_2O_4$	54·7	4·7	7·2	9·3	8·0	54·7	4·8	7·1	9·0	8·1
XI*n*	,,	—	—	7·1	9·3	8·5	—	—	7·1	9·0	8·1

[a] Examples *a*—*i* correspond to examples *a*—*i* of Part III,[1] Table 3.

[b] A, Fractional crystallisation of oxalates from ethanol. B, Base exchange chromatography. C, Chromatography on alumina. D, Preferential destruction of *cis*-isomer by treatment with acetic anhydride. E, Dehydration by hot sulphuric acid to give pure *trans*-isomer. F, Crystallisation of solid base.

[c] Solvent ethanol except when otherwise indicated. [d] All with decomp. except those marked *. [e] Solvent chloroform, followed by ethanol. [f] Solvent methanol. [g] Solvent ethyl acetate. [h] Solvent ethanol–ethyl acetate. [i] Solvent light petroleum (b. p. 40—60°). [j] Solvent methanol–ethanol. [k] Replaces the group R^1Ph. [l] In ethanol, except where indicated by ‡ when the solvent is water.

11·5%). Light absorption in 4×10^{-4}M-solution in EtOH: max. 255 mμ (log ε 4·35); in 4×10^{-5}M-solution in 5·5M-HCl: max. 249 mμ (log ε 4·15).

(b) *By alumina chromatography of bases* (*Table* 3, *method* C). The mixture of bases (10 g.), dissolved in light petroleum (b. p. 40—60°; 100 ml.), was adsorbed on alumina (400 g.; column 5 cm. in diam.) and eluted with benzene, the eluate being collected in 2-l. portions. The progress of the separation was followed by absorption spectrum and m. p. of the oxalate of the separate portions. From the head fractions (1—3) was obtained pure *cis*-isomer oxalate (1·3 g.). After elution with 20 l. of benzene, the column was stripped with chloroform to give base (4·2 g.) from which, after two crystallisations, pure *trans*-isomer oxalate (2·3 g.) was obtained.

Oxidation of cis- *and* trans-1-p-*Chlorophenyl*-1-2′-*pyridyl*-3-*pyrrolidinoprop*-1-*ene*.—(i) *cis*-Isomer oxalate (5 g.), in glacial acetic acid (150 ml.), was added to a mixture of chromium trioxide (36 g.), water (25 ml.), and glacial acetic acid (240 ml.), and the whole heated on the steam-bath for 5 min. The mixture was poured on ice, basified with ammonia, and extracted thrice with ether. Evaporation of the ether gave a colourless solid (2·7 g., 96%). Crystallisation from light petroleum (b. p. 40—60°) gave 2-p-*chlorobenzoylpyridine* (1·9 g., 68%), m. p. 64°

(Found: C, 66·2; H, 3·5; N, 6·6; Cl, 16·6. $C_{12}H_8ONCl$ requires C, 66·2; H, 3·7; N, 6·4; Cl, 16·4%); its p-*nitrophenylhydrazone* formed needles (from ethanol), m. p. 186° (Found: C, 61·5; H, 3·8; Cl, 10·4. $C_{18}H_{13}O_3N_4Cl$ requires C, 61·3; H, 3·7; Cl, 10·1%). This was identical (m. p. and mixed m. p. as base and as *p*-nitrophenylhydrazone) with a synthetic specimen prepared by reaction of pyridyl-lithium with *p*-chlorobenzonitrile.

(ii) Oxidation of *trans*-isomer base (1·0 g.) by the same method gave the same ketone (0·62 g., 85%), m. p. and mixed m. p. 63—64° (*p*-nitrophenylhydrazone, m. p. and mixed m. p. 186°).

(iii) *trans*-Isomer base (4 g.) was dissolved in water (20 ml.) by the dropwise addition of 2N-hydrochloric acid till just acid to Congo-red, and potassium permanganate (4·25 g.) in water (250 ml.) was added with stirring during 1 hr. The mixture was distilled in steam. The ketone solidified in the distillate and after filtration and drying (1·4 g., 48%) had m. p. and mixed m. p. 63°.

(iv) *cis*-Isomer base (4·0 g.), similarly oxidised, gave the ketone (0·9 g., 31%), m. p. and mixed m. p. 63—64°.

Hydrogenation of cis- *and* trans-1-p-*Chlorophenyl*-1-2′-*pyridyl*-3-*pyrrolidinoprop*-1-*ene*.—(i) *trans*-Isomer base (5 g.) in glacial acetic acid (50 ml.) was hydrogenated in the presence of palladium–charcoal (1·0 g.). Absorption (400 ml.) ceased after 48 hr. After filtration and removal of the solvent *in vacuo*, the gummy acetate was converted into base and thence into oxalate (5·6 g., 84%), m. p. 144—145°. After two crystallisations from ethanol the 1-*p*-chlorophenyl-1-2′-pyridyl-3-pyrrolidinopropane oxalate (4·8 g., 72%) had m. p. 146—147° [Part III,[1] (VIII*g*), gives m. p. 148—149°]. The oily base prepared from it had n_D^{19} 1·570.

(ii) *cis*-Isomer base (5 g.), similarly reduced with palladium–charcoal (2 g.), absorbed hydrogen (430 ml.) for 24 hr. The crude oxalate (5·5 g., 82%) had m. p. 143—144°, raised on crystallisation to m. p. 146—147°, unchanged on admixture with previous sample; the base had n_D^{19} 1·570.

1-*Aryl*-1-2′-*pyridyl*-3-(*tertiary amino*)*propan*-1-*ols* (I and XII).—Five alcohols (Table 2) not previously described were prepared by the method give in Part III [1] from the corresponding aryl 2-pyrrolidinoethyl ketones (Table 1).

Dehydration of the Alcohols (I) *to Mixtures of the* trans- *and* cis-1-*Aryl*-1-2′-*pyridyl*-3-(*tertiary amino*)*prop*-1-*enes* (X and XI).—With some exceptions noted below, dehydration of the alcohols (I) to mixtures of the *trans*- and *cis*-allylamines (X and XI) was effected by 5 times the weight of aqueous sulphuric acid (85% v/v) at 100° for 15—20 min. and working up as previously described,[1] except that the oily mixtures of isomeric allylamines were not distilled. Examples (*g*) and (*l*) (Table 3) were similarly prepared by using concentrated sulphuric acid, and examples (*m*) and (*n*) by aqueous sulphuric acid (65% v/v) at 120° and 105° respectively.

Separation of the trans-(X) *and* cis-(XI) *Isomers* (Table 3).—(a) *By fractional crystallisation* (Table 3, method A). Examples (*d*), (*h*), and (*i*) were separated by direct fractional crystallisation of the oxalates from ethanol as described above for example (*g*), the *trans*-isomer being less soluble. The isomers of example (*i*) resembled those of example (*g*) in showing a large difference in solubility and the recovery of separated pure isomers was high. The isomers of examples (*d*) and (*h*) did not differ greatly in solubility, and recovery of separated isomers was low. Examples (*a*) and (*f*) were separated similarly, the *cis*-isomer being the less soluble. Example (*e*) was separated by the following procedure: a cold saturated alcoholic solution of the mixed isomeric oxalates was evaporated to half volume and allowed to cool somewhat. While still warm a crop of plates separated and was filtered off. The filtrate shortly deposited a mass of needles which was collected. The plates were recrystallised to give pure cis-*isomer oxalate*, m. p. 174—175° [base, m. p. 61—62° after crystallisation from light petroleum (b. p. 40—60°)], and the needles to give pure trans-*isomer oxalate*, m. p. 182—183°. Examples (*b*), (*c*), and (*j*) resisted separation by crystallisation.

Crystalline form was a reliable guide to the course of separation in some cases, *e.g.*, the separation of examples (*e*), (*g*), and (*i*), in all of which the *trans*-form crystallised in needles and the *cis*-form in plates, but in other cases was unhelpful or misleading. Many of the isomer oxalates were found to be dimorphous, *e.g.*, (XI*e*) could be obtained at will as needles or plates, depending on whether it was left to crystallise in the presence or absence of a trace of undissolved solid. Separations were more reliably followed by m. p. and ultraviolet spectrum.

(b) *By base-exchange chromatography* (Table 3, method B). Examples (*b*), (*c*), (*g*), (*k*), (*l*), (*m*), and (*n*) were separated on columns of sulphonated polystyrene of low cross-linkage in aqueous ethanol by displacement development using aqueous-ethanolic ammonia.[13]

(c) *By chromatography on alumina* (Table 3, method C). Example (*l*) was separated by this method, as described above for example (*g*), the eluates being light petroleum (b. p. 40—60°), and light petroleum (b. p. 40—60°) containing chloroform in increasing proportion (up to 25% v/v).

Behaviour towards Acetic Anhydride of cis- *and* trans-1-p-*Chlorophenyl*-1-2′-*pyridyl*-3-*pyrrolidinoprop*-1-*ene*.—(i) *trans*-Isomer base (1·0 g.) was boiled in acetic anhydride (15 ml.) for ½ hr. The excess of reagent was distilled off *in vacuo*, the oily residue was dissolved in water, the base was liberated with ammonia and taken into ether, and the ether was removed. The oily base (0·8 g.) solidified on seeding and gave oxalate (0·9 g.), m. p. 184°, unchanged on admixture with *trans*-isomer oxalate.

(ii) *cis*-Isomer base (2·0 g.), similarly treated, gave, after removal of the excess of reagent, a viscous dark oil from which pale yellow needles separated. These were filtered off and washed with ether. From the dark filtrate, treated as in (i), no solid oxalate separated or could be isolated by dilution with ether. The yellow needles (0·4 g.) after crystallisation from ethanol gave 3-*acetyl*-1-p-*chlorophenylpyrrocoline* as pale yellow needles, m. p. 173—174°, not depressed on admixture with authentic material prepared as described below [Found: C, 71·4; H, 4·7; N, 5·0; Cl, 13·0; Ac, 15·5%; *M* (Rast), 276. $C_{16}H_{12}ONCl$ requires C, 71·3; H, 4·5; N, 5·2; Cl, 13·2; Ac, 16·0%; *M*, 269·5].

3-*Acetyl*-1-p-*chlorophenylpyrrocoline* (IV).—A mixture of 2-4′-chlorobenzylpyridine [15] (10 g.) and acetic anhydride (60 ml.) was heated (pressure tube) at 280° for 7 hr. The dark crystalline product (9 g.) was filtered from excess of anhydride and distilled. The yellow distillate (b. p. 215—235°/0·1 mm.) solidified and after crystallisation from ethanol gave the compound (IV) (5·2 g.), m. p. 172—173° not depressed on admixture with the sample described above.

Differential Acetic Anhydride Degradation of Mixed Isomers (X) *and* (XI) *with Isolation of* trans-*Isomer* (X) (Table 3, method D).—*Examples*: (i) A mixture of (X*g*) and (XI*g*) oxalates (10 g.) was boiled under reflux with acetic anhydride (160 ml.) for ½ hr. After working up as above, solid oxalate (2·8 g.) was obtained by dilution with ether, and after one crystallisation from ethanol (2·3 g.) had m. p. 184°, unchanged on admixture with (X*g*) oxalate.

(ii) A mixture of (X*c*) and (XI*c*) bases (30 g.) was boiled under reflux with acetic anhydride (150 ml.) for 15 min. and worked up as above. Dilution with ether gave a semisolid oxalate which after two crystallisations from ethanol gave (X*c*) oxalate (7·5 g.), m. p. 164—165°.

(iii) A mixture of (X*b*) and (XI*b*) oxalates (partially separated by crystallisation and having m. p. 135—140°) (2 g.) and acetic anhydride (30 ml.) was treated as above. After crystallisation from ethanol (X*b*) oxalate (1·2 g.), m. p. 130—131°, was obtained.

(iv) A mixture of (X*j*) and (XI*j*) crude bases (4·8 g.) and acetic anhydride (40 ml.) was boiled under reflux for 10 min. and worked up as above. The basic product (2·3 g.) was distilled and the fraction boiling at 134—136°/0·02 mm. (1·5 g.) was converted into the oxalate. Crystallisation from methanol–ethanol gave (X*g*) oxalate (1·0 g.), m. p. 162—163°.

Effect of Temperature and Strength of Sulphuric Acid on the Proportions of cis- *and* trans-*Isomers obtained from* 1-p-*Chlorophenyl*-1-2′-*pyridyl*-3-*pyrrolidinopropan*-1-*ol*.—*Examples*: (i) The alcohol (10 g.) was dissolved in concentrated sulphuric acid (100 ml.) below 10°. After a further 2 hr. below 10°, the mixture was worked up as described above. The oily base (9·0 g., 95%) did not crystallise on being seeded with *trans*-isomer base, and was converted into crude oxalate (9·8 g., 78%) (m. p. 148—152°), which after numerous crystallisations gave pure *trans*-isomer oxalate (1·7 g., 13·5%), m. p. 184°.

(ii) The alcohol (10 g.) was added during 5 min. to concentrated sulphuric acid (100 ml.) at 200°, and the mixture was held at 200° for a further 5 min. After working up as in (i), solid *trans*-isomer base (9·2 g., 98%), m. p. 55—58°, was obtained, which gave *trans*-isomer oxalate (10·2 g., 81%), m. p. 184°.

(iii) The alcohol (5 g.) was heated similarly with concentrated sulphuric acid (25 ml.) at 250°. On working up as in (i), solid *trans*-isomer base (2·3 g.) was obtained [oxalate (2·2 g., 35 %), m. p. 184°].

(iv) *cis*-Isomer base (9 g.) was heated in concentrated sulphuric acid (50 ml.) at 160° for 10 min. After working up as in (i), there was obtained solid *trans*-isomer base (9·0 g.) [oxalate (9·8 g.), m. p. 183—184°].

Numerous similar experiments were carried out for periods of heating of 10 min. and 3 hr.,

[14] Houben-Weyl, "Methoden der Organischen Chemie," 4th edn., 1955, Vol. III, Part 2, p. 667.
[15] Panizzon, *Helv. Chim. Acta*, 1944, **27**, 1748.

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the temperature being varied by intervals of 20°, and the strength of the sulphuric acid by 20% decrements. The results are tabulated as the limiting temperatures (with a possible −20° error) above which exclusive formation of *trans*-isomer occurs, the criteria for exclusive formation being (i) the crude base forming a hard solid, and (ii) the crude oxalate having m. p. >180°.

H_2SO_4 (%)	100	80	60
Limiting temp. : 10 min.	160°	180°	200° (superheated)
3 hr.	120°	140°	160°

A second set of experiments defined approximately the time necessary to effect complete conversion into *trans*-isomer in concentrated sulphuric acid at different temperatures.

Temp.	200°	160°	120°	100°	80°
Time of 100% conversion	<2 min.	<10 min.	1 hr.	>3, <6 hr.	>21 hr.

Behaviour of Other Alcohols on Vigorous Sulphuric Acid Treatment (Table 3, method E).—(i) The alcohol (I; $R^1 = H$, $NR^2R^3 = N<[CH_2]_4$) (5 g.) was heated with concentrated sulphuric acid (25 ml.) at 200° for 10 min., poured on ice, and treated with excess of ammonia; no insoluble material separated.

(ii) The alcohol (I; $R^1 = H$, $NR^2R^3 = N<[CH_2]_4$) (2 g.) was heated in concentrated sulphuric acid (10 ml.) at 150° for 5 min. Working up as above gave (X*c*) oxalate (0·5 g.), m. p. and mixed m. p. 163—164°.

(iii) The alcohol (I; $R^1 = Cl$, $NR^2R^3 = NMe_2$) (8·0 g.) was heated with concentrated sulphuric acid (50 ml.) at 180° for 10 min. It gave pure (X*e*) oxalate (6·0 g.), m. p. and mixed m. p. 182—183°.

(iv) The alcohol (I; $R^1 = H$, $NR^2R^3 = NMe_2$) (3 g.), heated with concentrated sulphuric acid (20 ml.) at 140° for 5 min., gave (X*a*) oxalate (1·3 g.), m. p. and mixed m. p. 178—179°.

(v) The alcohol (I; $R^1 = Br$, $NR^2R^3 = N<[CH_2]_4$) (10 g.) was heated in concentrated sulphuric acid (20 ml.) at 185° for 10 min. Working up gave an oil which on crystallisation from light petroleum (b. p. 60—80°) gave the compound (X*l*) (6·5 g.), m. p. 90—91°.

(vi) The alcohol (XII) (2·0 g.) was heated in aqueous sulphuric acid (85% v/v; 6 ml.) on the steam-bath for 6 min. On working up, this gave (X*n*) oxalate (1·1 g.), m. p. 149°.

Geometrical Isomers of 1-p-*Chlorophenyl*-1-*phenyl*-3-*pyrrolidinoprop*-1-*ene*.—1-p-*Chlorophenyl*-1-*phenyl*-3-*pyrrolidinopropan*-1-*ol* (VII) was prepared by the reaction of phenylmagnesium bromide with 4-chloro-β-pyrrolidinopropiophenone [1] and after crystallisation from light petroleum (b. p. 60—80°) had m. p. 118—120° (Found: C, 72·2; H, 7·0; N, 4·3; Cl, 11·2. $C_{19}H_{22}ONCl$ requires C, 72·3; H, 7·0; N, 4·4; Cl, 11·3%). The alcohol (10 g.) was dehydrated by boiling concentrated hydrochloric–glacial acetic acid as described in Part I.[16] The crude hydrochloride obtained on evaporation to dryness crystallised from ethanol–ethyl acetate, then from ethanol, to give that *isomer* (IX) of 1-p-*chlorophenyl*-1-*phenyl*-3-*pyrrolidinoprop*-1-*ene hydrochloride* showing a styrene-like spectrum (Fig. 3) (3·6 g.; m. p. 219—221°) (Found: Cl, 20·9. $C_{19}H_{21}NCl_2$ requires Cl, 21·3%). The ethanol–ethyl acetate filtrate, after concentration, deposited crystals which, after several recrystallisations from ethanol–ethyl acetate, gave that *isomer* (VIII) showing a *p*-chlorostyrene-like spectrum (Fig. 3) [3·0 g.; m. p. 165—167° (decomp.)] (Found: Cl, 21·7%).

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[16] Adamson, *J.*, 1949, S144.

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446. *The H_0 Acidity Function in Aqueous Dioxan and in Methanol.*

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The degrees of protonation of three indicators, *o*-nitroaniline, *p*-nitroaniline, and 4-chloro-2-nitroaniline have been measured with various concentrations of perchloric acid in 60% water–40% dioxan and in 40% water–60% dioxan. Similar measurements have been made with methanesulphonic acid in methanol. The results indicate that for the two aqueous solvents the H_0 concept is applicable and values of H_0 for solutions containing up to about 4N-perchloric acid have been calculated. For methanesulphonic acid in methanol, however, the concept appears of doubtful value. The rates of hydrolyses of sucrose and of ethyl acetate in 40% water–60% dioxan containing perchloric acid have been shown to depend on the acidity function and stoichieometric acidity respectively. It is concluded that the Zucker–Hammett criterion of mechanism can be usefully applied to 40% and 60% aqueous dioxan solvents.

In 1939 Zucker and Hammett [1] suggested that for acid-catalysed reactions of initially uncharged substances in water, bimolecular and unimolecular mechanisms (*A*2 and *A*1, respectively, in Day and Ingold's terminology [2]) could be distinguished according to whether the logarithm of the first-order rate coefficient increases linearly with the logarithm of the stoicheiometric acidity or with Hammett's acidity function H_0. This criterion has now been widely used in the study of acid-catalysed reactions and mechanistic assignments based on its use have, in general, been in accord with expectations derived from other evidence.

Many reactions, for reasons of solubility, cannot be conveniently studied in water, and there is, therefore, a need for measurements establishing the H_0 scale for solvents other than water. However, for solvents of low dielectric constant it is probable that a H_0 scale constructed from indicator measurements in the normal way would have little generality or utility. It is necessary, therefore, to choose solvents, of high dielectric constant, in which organic substrates might be expected to be fairly soluble. Accordingly we have carried out measurements designed to test the validity of the H_0 concept and its kinetic utility in 40% and 60% aqueous dioxan and in methanol.

A number of previous studies of solvents other than water have been made and although in no case has the generality of the H_0 scale been firmly established, good correlations of reaction rates with indicator acidities have been reported. Gebhard and Adams,[3] for example, studied the rearrangement of benzopinacol to the corresponding pinacone in slightly aqueous acetic acid containing small concentrations of perchloric acid, and found that both the direct conversion and the conversion *via* an intermediate epoxide were dependent on H_0. The decomposition of trioxan has been studied [4] in both acetic acid and water, and the reported correlation of the rates through the H_0 values is good.

Eaborn [5] studied the acid-catalysed cleavage of a silane derivative in aqueous methanol and in aqueous dioxan and found good correlations between rates and H_0 values as measured by a single indicator (*p*-nitroaniline). More recently, however, he reported that in 27% aqueous methanol the plot of the logarithm of the indicator ratio for *p*-nitroaniline against that for *o*-nitroaniline does not give unit slope.[6]

An important contribution was made by Braude and Stern [7] who measured H_0 for two indicators, *p*- and *m*-nitroaniline, at two acid concentrations for a variety of solvents,

[1] *J. Amer. Chem. Soc.*, 1939, **61**, 2791.
[2] Day and Ingold, *Trans. Faraday Soc.*, 1941, **37**, 686.
[3] Gebhard and Adams, *J. Amer. Chem. Soc.*, 1954, **76**, 3925.
[4] Walter and Chadwick, *Ind. Eng. Chem.*, 1947, **39**, 974.
[5] Eaborn, *J.*, 1953, 3148.
[6] *Idem*, *J.*, 1945, 1436.
[7] Braude, *J.*, 1948, 1971; Braude and Stern, *ibid.*, pp. 1976, 1982.

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namely, ethanol, acetone, dioxan, and their aqueous mixtures. Although the results do not establish the validity of the H_0 concept in any of the solvents used, and have been criticised by Gutbezahl and Grumwald [8] on the grounds that for aqueous ethanol their criterion, based on the use of their activity postulate, shows the non-existence of an acidity function, significant correlations between reaction rates and indicator measurements were nevertheless obtained.

Recently Kreevoy [9] examined the H_0 scale in 50% aqueous dioxan containing perchloric acid, essentially by comparing the behaviour of an indicator, 4-chloro-2-nitroaniline, with the kinetic behaviour of four acetals and ketals. These results will be discussed later.

Results

(a) *Indicator Measurements.*—The ratios of unprotonated to protonated base ($[B]/[BH^+]$) $= I$ for three indicators were determined by spectrophotometric means at various acid strengths in 60% (v/v) and 40% aqueous dioxan and in methanol. Perchloric acid was used in the two aqueous solvents, and the solutions were made up so that the ratio of water to dioxan, in terms of volumes added together, was constant for each solvent irrespective of acidity. The choice of acid for methanol presented some difficulty. Hydrochloric, nitric, and sulphuric acids were found to react too fast with the solvent; the use of perchloric acid required the inconvenient preparation and use of the anhydrous acid. Methanesulphonic acid, which would be expected to be a reasonably strong acid in methanol and to produce only a slow esterification, was found to be suitable.

Values of H_0 were calculated from the equation:

$$H_0 = \log I + pK_B \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (1)$$

where

$$pK_B = -\log \frac{a_{H^+} a_B}{a_{BH^+}} \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (2)$$

The values of pK_B used in the calculation were referred to water as solvent and were those recently reported by Paul and Long; [10] they are a little different from the values originally used by Hammett and Deyrup [11] and amended by Hammett and Paul.[12] Table 1 gives the collected values

For each of the two aqueous solvents the H_0 values for the three indicators form a continuous curve of H_0 against stoicheiometric acidity, *i.e.*, the separate curves for the three indicators overlap without discontinuity. Figs. 1 and 2 show the curves, judged visually as representing the best fit, for the two aqueous solvents. It will be seen that some of the points obtained by using *o*-nitroaniline at low acidities are significantly displaced from the curves. These points, however, are subject to relatively large experimental errors since they represent measurements of small degrees of protonation. Within the limits of accuracy of the experimental procedure, therefore, the values of H_0 may be taken as independent of the nature of the indicator used.

In methanol solvent, however, the situation is different. A continuous curve can be drawn, as in Fig. 3, only if the pK_B value for 4-chloro-2-nitroaniline is taken as $-1{\cdot}23$ instead of $-1{\cdot}03$, the true value. The values of H_0 so obtained are shown in Table 1 in parentheses and have been used in constructing Fig. 3.

By extrapolating the plots of $-\log c_{H^+} I$ against c_{H^+} to infinite dilution, the data can be used to find approximate values of the ionisation constants (pK_B) of the conjugate acids of the three indicators in the various solvents. The values so obtained are listed in Table 2 and can be used, if desired, to find H_0 values referred to infinite dilution in the particular solvent as standard state.

(b) *Kinetic Measurements.*—The rates of hydrolysis of sucrose and of ethyl acetate in 40% water–60% dioxan at various concentrations of perchloric acid were measured, by polarimetric

[8] Gutbezahl and Grunwald, *J. Amer. Chem. Soc.*, 1953, **75**, 559, 565.
[9] Kreevoy, *J. Amer. Chem. Soc.*, 1956, **78**, 4237.
[10] Paul and Long, *Chem. Rev.*, in the press.
[11] Hammett and Deyrup, *J. Amer. Chem. Soc.*, 1932, **54**, 2721.
[12] Hammett and Paul, *ibid.*, 1934, **56**, 827.

and dilatometric methods respectively, at 25°. The results are given in Table 3. It will be seen that the acid concentrations used were in the range where the H_0 values change much more rapidly than the corresponding values of $-\log c_{H^+}$.

FIG. 1. *H_0 for perchloric acid in 60% water–40% dioxan.*

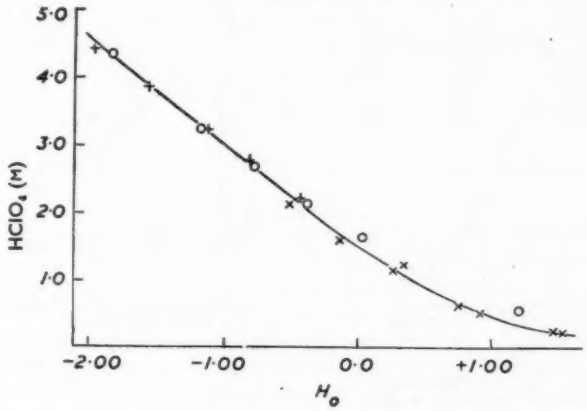
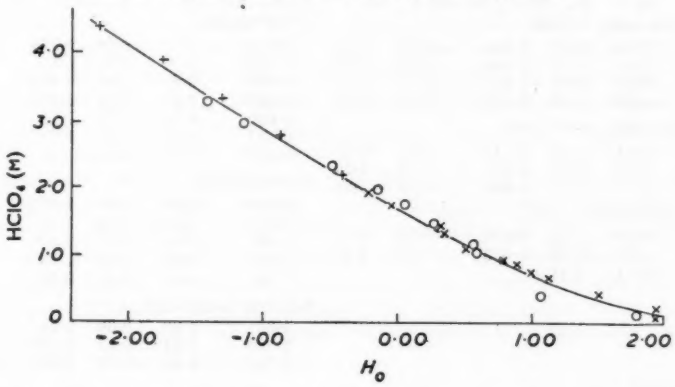


FIG. 2. *H_0 for perchloric acid in 40% water–60% dioxan.*

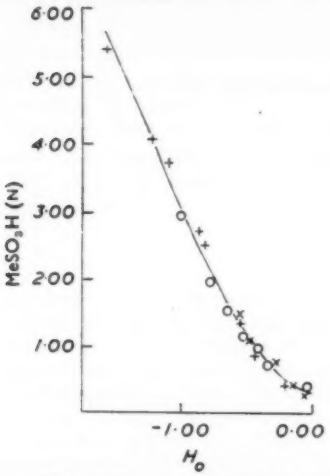


FIGS. 1 *and* 2. ×, p-*Nitroaniline*; ○, o-*nitroaniline*; +, 4-*chloro*-2-*nitroaniline*.

The rate of hydrolysis of ethyl acetate is clearly proportional to the stoicheiometric acidity, *i.e.*, k_2 is sensibly constant and log k_1 plotted against $-\log c_{H^+}$ gives a straight line of unit slope. The rate of hydrolysis of sucrose, however, increases very much more rapidly, by a factor of 6·6 over the range of acidities studied, than does the stoicheiometric acid concentration and is clearly dependent on H_0. A plot of log k_1 against H_0 for the sucrose reaction gives a straight line of nearly unit slope (1·02). This line (○), together with a plot (×) of the values obtained by Leininger and Kilpatrick [13] with hydrochloric acid in water as solvent, is shown in Fig. 4. The broken line indicates the expected curve if the rate in 40% aqueous dioxan were linearly dependent on stoicheiometric acidity.

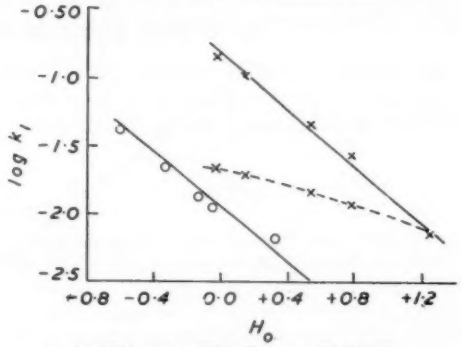
[13] Leininger and Kilpatrick, *J. Amer. Chem. Soc.*, 1938, **60**, 2891.

FIG. 3. *H_0 for methanesulphonic acid in methanol.*



×, p-*Nitroaniline*; ○, *o-nitroaniline*; + *4-chloro-2-nitroaniline (adjusted to fit the curve).*

FIG. 4. *Hydrolysis of sucrose at 25°.*



×, *in 40% water–60% dioxan with* $HClO_4$.
○, *in water with* HCl.[13]
Broken curve is that expected if reaction followed molar acidity.

TABLE 1.

(a) 60% *Water–40% dioxan.*

$HClO_4$ (M)	log *I*	H_0	$HClO_4$ (M)	log *I*	H_0
p-Nitroaniline, $pK_B = 0·99$					
0·217	0·53	1·52	1·086	−0·70	0·29
0·222	0·51	1·50	1·108	−0·66	0·33
0·543	−0·07	0·92	1·63	−1·11	−0·12
0·653	−0·23	0·76	2·172	−1·48	−0·49
o-Nitroaniline, $pK_B = -0·29$					
0·543	1·51	1·22	2·715	−0·48	−0·77
1·629	0·32	0·03	3·25	−0·86	−1·15
2·172	−0·10	−0·39	4·344	−1·55	−1·84
4-Chloro-2-nitroaniline, $pK_B = -1·03$					
2·22	0·61	−0·42	3·878	−0·53	−1·56
2·77	0·25	−0·78	4·423	−0·92	−1·95
3·324	−0·11	−1·14			

(b) 40% *Water–60% dioxan.*

$HClO_4$ (M)	log *I*	H_0	$HClO_4$ (M)	log *I*	H_0
p-Nitroaniline					
0·195	0·95	1·94	0·976	−0·21	0·78
0·230	0·96	1·95	1·15	−0·45	0·54
0·460	0·50	1·49	1·313	−0·61	0·38
0·586	0·25	1·24	1·464	−0·67	0·32
0·689	0·14	1·13	1·75	−1·03	−0·04
0·781	0·01	1·00	1·95	−1·21	−0·22
0·875	−0·11	0·88			
o-Nitroaniline					
0·195	2·09	1·80	1·72	0·34	0·05
0·587	1·37	1·08	1·95	0·08	−0·21
1·09	0·88	0·59	2·30	−0·21	−0·50
1·15	0·85	0·56	2·93	−0·85	−1·14
1·464	0·56	0·27	3·28	−1·13	−1·42
4-Chloro-2-nitroaniline					
1·641	1·03	0·00	3·28	−0·28	−1·31
2·188	0·61	−0·42	3·849	−0·72	−1·75
2·735	0·16	−0·87	4·376	−1·20	−2·23

(c) *Methanol*

$Me·SO_3H$ (M)	log *I*	H_0	$Me·SO_3H$ (M)	log *I*	H_0
p-Nitroaniline					
0·367	−1·05	−0·06	1·101	−1·47	−0·48
0·441	−1·15	−0·16	1·468	−1·54	−0·55
0·734	−1·28	−0·29			
o-Nitroaniline					
0·380	0·24	−0·05	1·52	−0·34	−0·63
0·76	−0·05	−0·34	1·94	−0·48	−0·77
0·97	−0·14	−0·43	2·91	−0·68	−0·97
1·14	−0·22	−0·51			
4-Chloro-2-nitroaniline					
0·441	1·05	0·02 (−0·18)	2·50	0·42	−0·61 (−0·81)
0·882	0·80	−0·23 (−0·43)	2·70	0·38	−0·65 (−0·85)
1·33	0·69	−0·34 (−0·54)	3·69	0·15	−0·88 (−1·08)
1·373	0·68	−0·35 (−0·55)	4·05	0·03	−1·00 (−1·20)
			5·40	−0·30	−1·33 (−1·53)

TABLE 2.

	60% Aqueous dioxan	40% Aqueous dioxan	Methanol
p-Nitroaniline	0·00	−0·34	1·55
o-Nitroaniline	−1·40	−1·58	0·20
4-Chloro-2-nitroaniline	−2·08	−2·35	−0·67

TABLE 3.*

$HClO_4$ (M)	10^2k_1	10^2k_2	H_0	$HClO_4$ (M)	10^2k_1	10^2k_2	H_0
(1) Sucrose hydrolysis				(2) Ethyl acetate hydrolysis			
0·591	0·743	1·26	1·25	0·470	0·246	0·523	1·43
0·948	2·8	2·95	0·77	0·948	0·54	0·570	0·77
1·171	4·64	3·96	0·53	1·860	1·17	0·630	−0·15
1·578	10·4	6·60	0·13	2·230	1·31	0·588	−0·49
1·740	14·5	8·33	−0·03				

* k_1 is the first-order rate coefficient in min.$^{-1}$. k_2 is k_1/c_{H^+} in min.$^{-1}$ mole^{-1} l.

DISCUSSION

For the acidity function concept to be applicable to a given solvent the activity coefficient ratio, f_B/f_{BH^+}, for a neutral base and its conjugate acid, must be essentially independent of the nature of the base. When this is true, values of H_0, calculated by equation 1 (and using pK_B values referring to water as solvent) from data obtained with different indicators, should depend only on acid concentration. If, as is usually the case, the indicators cover different ranges of acidities, the corresponding curves of H_0 against acid concentration should overlap without discontinuity. This is essentially the criterion originally used by Hammett and Deyrup.[11] In the present case the results for the two aqueous solvents satisfy this criterion and, within the limits imposed by the nature of the three amine indicators chosen, it may be concluded that the H_0 concept is applicable to both solvents.

On the other hand, the values of H_0 for methanesulphonic acid in methanol are not independent of the indicator used, and a continuous curve of H_0 against acidity cannot be drawn. However, if the pK_B value of one of the indicators (4-chloro-2-nitroaniline) is arbitrarily decreased by 0·2 unit, the major discontinuity in the curve is removed (Fig. 3), but this procedure has no theoretical significance and it must be concluded that in this system the H_0 concept has little generality.

The same conclusions emerge by plotting the logarithms of the indicator ratios (log I) for pairs of indicators at a series of acidity values. This procedure essentially determines whether, in the overlap region, the curves of log I against acidity for two indicators are parallel. If they are not, clearly no continuous curve for H_0 can be drawn. The test is rather a severe one for the present results since the overlap region for any two indicators necessarily includes the least accurate values of the indicator ratios. The slopes of the plots are given in Table 4, which also includes values obtained from Hammett and Deyrup's original data [11] for perchloric acid in water.

TABLE 4.

	Water	60% Aqueous dioxan	40% Aqueous dioxan	Methanol
Log I_A/log I_B	0·99	0·98	1·08	1·12
Log I_C/log I_B	1·03	1·06	0·97	0·84

A = *p*-nitroaniline; B = *o*-nitroaniline; C = 4-chloro-2-nitroaniline.

The results for perchloric acid in the two aqueous dioxan solvents are not much worse, on this test, than those for water. For methanesulphonic acid in methanol, however, the plots are not quite linear and the average slopes are significantly different from unity; this system clearly does not satisfy the test.

It must be pointed out that, although the results show that for the three indicators used an acidity function exists in aqueous dioxan, it is not our view that the same result would necessarily be obtained whatever indicators were used. In other words, the use of three indicators with similar structures is not sufficient to satisfy the very stringent criterion for

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the existence of an acidity function given by Gutbezahl and Grunwald.[8] It seems to us that the H_0 concept does not have complete generality in any solvent, and we regard the present results primarily as indicating the probable usefulness of the concept as a diagnostic tool for reactions occurring in aqueous dioxan.

The results for methanol, on the other hand, do not support the view that there is an acidity function in this solvent, but this may be partly due to the choice of acid, since large anions are known to produce abnormally large activity effects under certain conditions.[14] However, even if the H_0 values for methanol in Table 1 were true acidity-function values they would be of little interest to the kineticist, since the rate of change of H_0 is not very different from the rate of change of $-\log c_{H^+}$. For example, in the range 1—4M methanesulphonic acid, where $-\log c_{H^+}$ changes by 0·60, the change in H_0 is 0·77, whereas in 40% aqueous dioxan the corresponding change for perchloric acid is 2·66. Although the reasons for this behaviour are not known it illustrates the limitations of a comparison of the acidities of different solvents at fixed acid concentrations.

Our results are compared with those of other workers in Table 5, which gives H_0 values at M-acid in aqueous dioxan. Kreevoy's data, which have been adjusted so as to refer to infinite dilution in water as standard state, are not wholly consistent with ours; this may be partly due to his method of making up solutions which is such that the dioxan–water

TABLE 5.

Authors	Acid	60% of water	50% of water	40% of water
Braude and Stern	HCl	0·89	—	1·24
Kreevoy	$HClO_4$	—	0·33	—
This work	$HClO_4$	0·48	—	0·72

ratio varies with the acidity. Braude and Stern's results show that aqueous dioxan solutions of M-hydrochloric acid are less acidic than those of M-perchloric acid. For both acids, at this concentration, 40% dioxan solutions are the more strongly acidic, although, as can be seen by reference to Table 1, this situation is reversed for perchloric acid solutions above 2·25M.

The rate of hydrolysis of ethyl acetate in water has been shown by Bell, Dowding, and Noble [15] to follow stoicheiometric acidity. As can be seen from Table 3 the same result is obtained in 40% aqueous dioxan. The actual rates at corresponding acidities are not very different in the two solvents; 10^3k_2 is 7·8 and 5·6 min.$^{-1}$ mole^{-1} l., in water and 40% aqueous dioxan respectively. Application of the Brönsted equation to a mechanism involving attack by a water molecule on the conjugate acid of a substrate (S) in the rate-determining stage leads [16] to the equation:

$$k = k_2k_e[OH_3^+]\frac{f_Sf_{OH_3^+}}{f_T} \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (3)$$

where k is the experimental first-order rate coefficient, k_2 is the true rate coefficient for the rate-determining stage, *i.e.*, is the rate coefficient under the chosen standard-state conditions, all variation in the rate being taken up by the activity coefficients, k_e is the equilibrium constant for the protonation of the substrate (S), and T^+ refers to the transition state, which in this case contains a water molecule. The product k_2k_e should be independent of environment, and k will depend on $[OH_3^+]$ alone if the activity ratio term is constant. The results obtained indicate that for a change of solvent from water to 40% aqueous dioxan this condition is approximately fulfilled.

The rate of hydrolysis of sucrose in water is dependent on H_0.[17] In 40% aqueous dioxan the same dependence is observed, the slopes of the plots of $\log k_1$ against H_0 being virtually the same in the two cases. Hence, the clear-cut distinction between the mechanisms of hydrolyses of sucrose and of ethyl acetate in water is equally well shown in

[14] Long and McDevit, *Chem. Rev.*, 1952, **51**, 119.
[15] Bell, Dowding, and Noble, *J.*, 1955, 3106.
[16] Hammett, "Physical Organic Chemistry," McGraw-Hill Book Co., New York, 1940, p. 276.
[17] Ref. 16, p. 274.

aqueous dioxan, and this supports the view that the Zucker–Hammett criterion of mechanism may be usefully employed in aqueous dioxan solvents.

Kreevoy's results [9] on the hydrolysis of acetals and ketals indicate that these reactions in 50% aqueous dioxan also depend on the acidity function. However, his demonstration of the validity of the concept in this solvent involves the joint use of indicator and kinetic data. Our view is that the H_0 scale should be established by indicator measurements alone, as was done originally for water solution, and that the Zucker–Hammett hypothesis, since it involves additional assumptions, should be tested subsequently by kinetic methods.

The actual rates of hydrolysis of sucrose in 40% aqueous dioxan, at particular values of H_0, differ appreciably from those in water. The comparison is shown in Fig. 4,* from which it can be seen that the reaction in water is the slower by a factor of *ca.* 13·4. If a rate coefficient for the rate-determining step be defined in the usual way by

$$\text{Rate} = k'[\text{SH}^+] \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (4)$$

then combining it with equation (1) we have

$$\text{Rate} = k'[\text{S}]h_0k_\text{B} \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (5)$$

where H_0 is $-\log h_0$. Hence:

$$k_1 = k'h_0k_\text{B} \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (6)$$

where k_1 is the experimentally determined first-order rate coefficient for given acidity. For two different solvents with the same substrate and acidity-function value, the relative values of k' are given by the relative values of the experimental rate coefficients, k_1. This is independent of mechanism and of the assumptions involved in the Zucker–Hammett hypothesis and assumes only the validity of the H_0 concept in the solvents used. However, differentiation of mechanism requires the application of the Brönsted equation, and this leads for a unimolecular heterolysis of the conjugate acid of S to the equation: [18]

$$k = k_2k_e a_{\text{H}^+}f_\text{S}/f_{\text{T}^+}$$

f_{T^+} referring to the transition state, which in this case, does not contain a water molecule, and the other symbols having the same significance as before. In so far as $f_\text{S}/f_{\text{T}^+}$ is equal to $f_\text{B}/f_{\text{BH}^+}$, the logarithm of the rate coefficient should depend only on H_0,† k_2k_e being independent of the environment.[19] The failure of the rates in water and in aqueous dioxan to correlate through the H_0 values is surprising, expecially since the slopes of the log k–H_0 plots are very close to unity in both cases. However, no formal incompatability arises here since the unit slopes in the log k–H_0 dependence require not that $f_\text{S}/f_{\text{T}^+}$ shall equal $f_\text{B}/f_{\text{BH}^+}$ where B represents an indicator, but that their first derivatives with respect to acid concentration shall be the same over the range of acidities studied. Whether this condition, which is sufficient for diagnosis, holds more generally than the more extreme requirement of equality of the two activity ratios, can only be established by more attempts to correlate rates in different solvents through H_0 values.

Experimental

(a) *Materials.*—Commercial *o*-nitroaniline, *p*-nitroaniline, and 4-chloro-2-nitroaniline were recrystallised from water three times. Dioxan was purified as described by Vogel.[20] Methanesulphonic acid was twice distilled in an all-glass apparatus. Anhydrous methanol was obtained by distillation from a suspension of magnesium methoxide in absolute methanol.

Solutions of methanesulphonic acid in methanol were found to give constant titres, against alkali, over the period of the experiments.

* Leiniger and Kilpatrick's data refer to concentrations of sucrose similar to those used by us.

† For two different solvents this will be true providing, of course, that the H_0 values have been referred to the same standard state.

[18] Ref. 19, p. 275.

[19] Glasstone, Laidler, and Eyring, "The Theory of Rate Processes," McGraw-Hill Book Co., New York, 1941, p. 404.

[20] Vogel, "Practical Organic Chemistry," Longmans, Green and Co., London, 1948, p. 175.

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(b) *Solutions.*—The 40% water–60% dioxan solutions were made up as follows: 40 volumes of water and 60 volumes of dioxan were mixed together. An appropriate amount of 72% "AnalaR" perchloric acid, previously standardised against borax, was added. The volume of water in this amount of acid was calculated, and an amount of dioxan, such that the ratio of its volume to the volume of water present in the perchloric acid was 60 : 40, was then also added. This procedure ensured that, whatever the acid concentration, the amounts of water and dioxan remained in constant ratio. A similar procedure was used for the other aqueous solvent.

(c) *Indicator Measurements.*—An appropriate amount of indicator, usually giving a solution *ca.* 10^{-5} times the concentration of acid, was dissolved in the appropriate solvent, and the optical densities at four wavelengths across the absorption peak were measured with a Unicam S.P. 500 Spectrophotometer. At the wavelengths chosen, Beer's law was obeyed for all three indicators, and the completely protonated forms gave negligibly small absorptions.

(d) *Kinetic Measurements.—Hydrolysis of sucrose.* Each solution was made by dissolving sucrose (*ca.* 0·1—0·2 g. in 10 c.c.) in 40% water–60% dioxan containing a known concentration of perchloric acid. The reaction was followed by placing the solution in a polarimeter tube, at 25° (thermostat), and reading the rotatory power at suitable times. The following results, which are typical, were obtained with a solution 1·578M in perchloric acid.

Time (min.)	0	0·75	1·83	2·83	3·55	4·33
Rotation	0·519°	0·460°	0·385°	0·332°	0·295°	0·264°
k_1 (min.$^{-1}$)	—	0·112	0·110	0·104	0·103	0·099
Time (min.)	5·66	7·00	11·00	15·10	18·30	∞
Rotation	0·194°	0·142°	0·018°	−0·058°	−0·090°	−0·214°
k_1 (min.$^{-1}$)	0·104	0·103	0·105	0·103	0·097	—

Hydrolysis of ethyl acetate. Solutions of 40% water–60% dioxan containing known concentrations of perchloric acid were degassed by quick pumping on a filter pump. Portions (25 c.c.) were kept at 25°; freshly distilled ethyl acetate (*ca.* 0·5 c.c.) was added, the whole was mixed, and a tap dilatometer (of *ca.* 20 c.c. volume and with a capillary of 0·4 mm. bore) was filled by suction. Readings were commenced 10 min. after filling. Good first-order rate coefficients, calculated by Guggenheim's method,[21] were obtained in all cases.

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[21] Guggenheim, *Phil. Mag.*, 1926, **7**, 538.

447. *Colchicine and Related Compounds. Part XV.* Synthetic Studies.*

By G. L. BUCHANAN and J. K. SUTHERLAND.

5-Acetamido-4-oxo-2′ : 3′ : 4′-trimethoxybenzo*cyclo*heptene (IX) has been synthesised by two routes from purpurogallin.

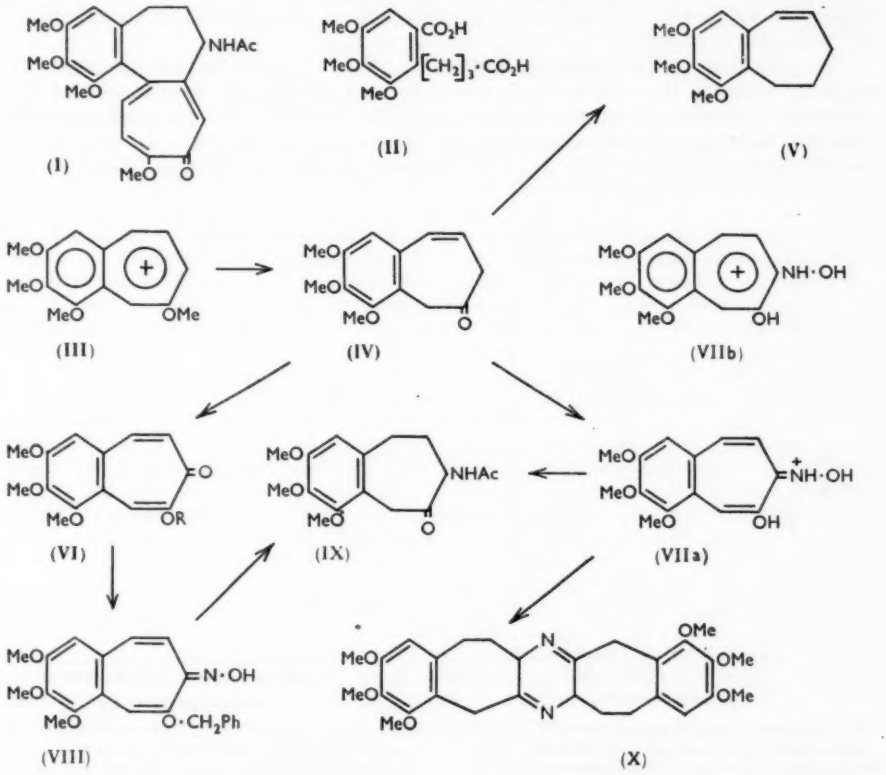
IN considering possible synthetical routes to colchicine (I) the ketone (IX) was chosen as the framework on which attempts to elaborate ring C would be made. This communication describes its synthesis.

Eschenmoser and his associates have described [1] the preparation of the tropylium cation (III) from purpurogallin, and its reduction to the ketone (IV). In our hands, the reduction proved to be capricious, and the expected ketone was separated from a non-ketonic oil by means of Girard's reagent P. That this oil was the styrene (V) followed from

* Part XIV, *J.*, 1955, 3864.

[1] Schaeppi, Schmidt, Heilbronner, and Eschenmoser, *Helv. Chim. Acta*, 1955, **38**, 1874.

its analysis, and the virtual identity of its ultraviolet absorption spectrum with that of the ketone (IV). This assignment was supported by its reduction to a dihydro-compound and its oxidation with cold aqueous potassium permanganate to the acid (II), previously synthesised by Haworth, Moore, and Pauson.[2] The styrene is apparently formed by a



Clemmensen-like reaction from the ketone (IV) rather than by an alternative path from the ion (III), for we were able to convert (IV) into (V) under the conditions of the original reaction.

From Eschenmoser's work,[1] it appeared likely that those reactions of the ketone (IV) which involved enolisation, would occur at the allylic rather than at the benzylic methylene group, and it seemed feasible therefore to introduce the nitrogen atom at this stage. The ketone was accordingly nitrosated, yielding a bright yellow oxime hydrochloride, for which we prefer the structure (VIIa). Catalytic reduction of this substance yielded the crude amino-ketone hydrochloride. When treated with alkali, this gave the dihydropyrazine (X), but when warmed with acetic anhydride, it afforded the acetamido-ketone (IX) which was characterised at its 2 : 4-dinitrophenylhydrazone. It was still necessary to prove the orientation of the nitrogen atom, and an attempt was made to hydrolyse the oxime hydrochloride (VIIa) to the known [1] tropolone (VI; R = H). With dilute hydrochloric acid and aqueous formaldehyde [3] a red product ($C_{15}H_{15}O_5N$) was isolated, but its structure has not been established. Its infrared spectrum shows neither O–H nor N–H bands.

[2] Haworth, Moore, and Pauson, *J.*, 1948, 1045.
[3] Caunt, Crow and Haworth, *J.*, 1951, 1313.

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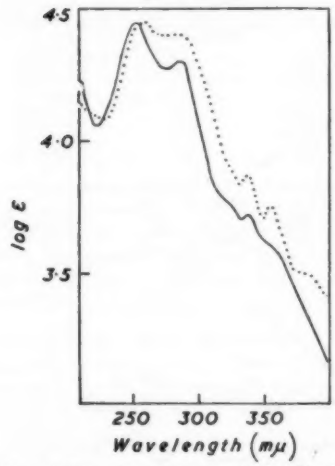
The structure of the acetamido-ketone (IX) was finally established by an unambiguous synthesis. The tropolone (VI; R = H), which can be obtained in poor yield from (IV), is already known [1] to be inactive towards carbonyl reagents, but its benzyl ether (VI; R = CH_2Ph) yielded an oxime (VIII) which on reduction in the presence of acetic anhydride afforded the ketone (IX). The latter was identified as its 2 : 4-dinitrophenylhydrazone, which was identical in m. p., mixed m. p., and infrared spectrum with the derivative described above.

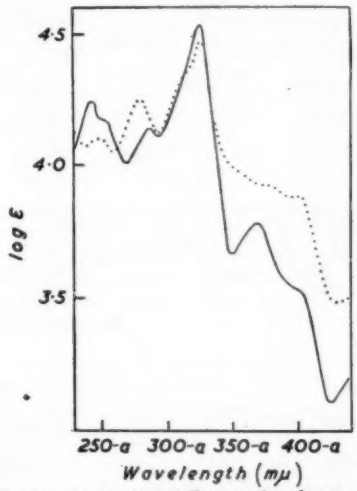
The structure of the oxime hydrochloride (VII) deserves further comment. We originally expected that the molecule would be most adequately represented as (VIIb), with minor contribution from the structure (VIIa). In fact, the ultraviolet spectrum (Fig. 1) is very close to that of the tropolone ether oxime (VIII), and quite distinct from that of the tropylium ion (III) (Fig. 2). More surprisingly, we have observed that after

FIG. 1



Full line, 4-*Benzyloxy*-5-*hydroxyimino*-2′ : 3′ : 4′-*trimethoxybenzo*cyclo*hepta*-1 : 3 : 6-*triene* (VIII).
Broken line, 4-*Hydroxy*-5-*hydroxyimino*-2′ : 3′ : 4′-*trimethoxybenzo*cyclo*hepta*-1 : 3 : 6-*triene hydrochloride* (VII).
(Solvent : ethanol.)

FIG. 2.



Full line, 4 : 2′ : 3′ : 4′-*Tetramethoxybenzo*cyclo*heptatrienylium sulphate* (III) (*a* = 0).
Broken line, 4-*Hydroxy*-5-*hydroxyimino*-2′ : 3′ : 4′-*trimethoxybenzo*cyclo*hepta*-1 : 3 : 6-*triene* (VII), *in the presence of alkali* (*a* = 10).
(Solvent : ethanol.)

basification of (VII), the spectrum of the product is strikingly similar to that of the tropylium ion (III) (Fig. 2). In order to point the similarity in Fig. 2, the oxime curve is drawn with a bathochromic displacement of 10 mμ.

EXPERIMENTAL

Reduction of 4 : 2′ : 3′ : 4′-*Tetramethoxybenzo*cyclo*heptatrienylium Sulphate* (III).—The reduction was carried out as previously described [1] and the oily product (5·98 g.) was separated with Girard's reagent P into the ketone (IV) (1·8 g.), m. p. 70—72° (*cyclo*hexane) [light absorption in ethanol; $\lambda_{max.}$ (log ε), 224 (4·4), 258 mμ (3·98)], and the styrene (V) (1·6 g.) which was filtered through neutral alumina in benzene, and distilled at 165—170°/0·08 mm. as a colourless oil (Found: C, 71·4; H, 7·6. $C_{16}H_{18}O_3$ requires C, 71·8; H, 7·7%) [light absorption in ethanol: $\lambda_{max.}$ (log ε), 223 (4·48), 263—264 mμ (4·05)].

2′ : 3′ : 4′-*Trimethoxybenzo*cyclo*heptene*.—The styrene (V) (300 mg.) rapidly absorbed 1 mol. of hydrogen in ethanol (15 ml.) in the presence of 2% Pd–$CaCO_3$ (200 mg.). After filtration,

concentration yielded the *dihydro-derivative*, b. p. 155—160° (bath)/0·3 mm., m. p. 44—48° (Found: C, 70·9; H, 7·7. $C_{14}H_{20}O_3$ requires C, 71·2; H, 8·5%). Light absorption: $\lambda_{max.}$ (log ε) 274 mμ (3·33).

Oxidation of 1′ : 2′ : 3′-*Trimethoxybenzo*cyclo*hepta*-1 : 3-*diene* (V).—The styrene (V) (500 mg.), in water (20 ml.), was shaken with portions of solid potassium permanganate until the mother liquors were permanently pink. After filtration, the filtrate was continuously extracted with ether for 4 hr. The product had m. p. 135—137° (from water) (Found: C, 56·6; H, 6·1%; equiv., 147. $C_{14}H_{18}O_7$ requires C, 56·4; H, 6·1%; equiv., 149). Light absorption: $\lambda_{max.}$ (log ε), 252 (4·02), 294 mμ (3·52). Mixed m. p. and infrared spectra showed it to be identical with a sample synthesised by Haworth's method.[2]

4-*Hydroxy*-5-*hydroxyimino*-2′ : 3′ : 4′-*trimethoxybenzo*cyclo*hepta*-1 : 3 : 6-*triene* (VII).—The ketone (IV) (3·6 g.) in ether (50 ml.) was cooled in ice and treated with dry hydrogen chloride, whilst pentyl nitrite (4 g.) in ether (20 ml.) was added dropwise. The yellow precipitate (2·69 g.) was filtered off; it had m. p. 206—208° (decomp.) (from ethanol) (Found: C, 53·6; H, 4·9; N, 4·5; Cl, 11·1%; equiv., 156. $C_{14}H_{16}O_5NCl$ requires C, 53·6; H, 5·1; N, 4·5; Cl, 11·3%; equiv., 157). Light absorption in ethanol: $\lambda_{max.}$ (log ε), 258 (4·46), 338—339 (3·87), 355 (3·75), 383 mμ (3·51); in alcoholic alkali, 241 (4·10), 271 (4·25), 321 (4·48), 391 (3·88), 460 mμ (3·57).

When the hydrochloride (184 mg.) was warmed for 5 min. with aqueous formaldehyde (40%; 1·5 ml.), with or without 5N-hydrochloric acid, and finally diluted, there was formed a flocculent red precipitate (68 mg.). The *product* crystallised in small red needles from ethanol; it had m. p. 168—170° (Found: C, 62·0; H, 4·9; N, 5·1. $C_{15}H_{15}O_5N$ requires C, 62·3; H, 5·2; N, 4·8%). Light absorption in ethanol: $\lambda_{max.}$ (log ε), 257 (4·45), 320 (4·54), 365 (4·12), 384 mμ (4·16); in acidified ethanol, 258 (4·42), 320 (4·54), 365 (3·99), 383 (4·01), 436 mμ (3·75).

5-*Acetamido*-4-*oxo*-2′ : 3′ : 4′-*trimethoxybenzo*cyclo*heptene* (IX).—(*a*) The hydrochloride (1 g.) in ethanol (20 ml.) containing Adams's platinum oxide catalyst (200 mg.) was shaken with hydrogen until 3 mols. had been absorbed, and was then filtered. Concentration of the filtrate yielded a dark glass which was warmed on the steam-bath for 10 min. with acetic anhydride (5 ml.), and concentrated *in vacuo*. The resulting dark oil afforded the *ketone* (IX) (617 mg.), m. p. 157—159°, as needles from acetone (Found: C, 62·6; H, 6·3; N, 4·9; MeO, 30·0; AcO, 13·5. $C_{16}H_{21}O_5N$ requires C, 62·5; H, 6·8; N, 4·6; 3MeO, 30·3; 1AcO, 14·0%). Light absorption: $\lambda_{max.}$ (log ε), 278—280 mμ (3·17) in ethanol; ν 1710 cm.$^{-1}$, in Nujol. It gave a 2 : 4-*dinitrophenylhydrazone*, m. p. 260—261° (decomp.), as yellow prisms from acetic acid (Found: C, 54·5; H, 5·1; N, 14·5. $C_{22}H_{25}O_8N_5$ requires C, 54·2; H, 5·1; N, 14·4%).

When a small portion of the above glass, in ethanol, was treated with 5N-sodium hydroxide solution, a white precipitate formed. Rapid crystallisation from ethanol gave the *dihydropyrazine* (X) as prisms, m. p. 230° (decomp.) (Found: C, 67·8; H, 7·1; N, 5·4. $C_{28}H_{34}O_6N_2$ requires C, 68·0; H, 6·9; N, 5·7%). Light absorption in ethanol: $\lambda_{max.}$ (log ε), 278 mμ (3·47).

(*b*) The hydroxyimino-ether (VIII) (39 mg.) in acetic anhydride (2 ml.) was shaken with hydrogen in the presence of Adams's platinum oxide catalyst (11 mg.). After the absorption of 4 mols. of hydrogen the solution was filtered. Concentration gave an oil which furnished a 2 : 4-dinitrophenylhydrazone, identical in m. p. and mixed m. p. and in its infrared spectrum with that described above.

4-*Benzyloxy*-5-*hydroxyimino*-2′ : 3′ : 4′-*trimethoxybenzo*cyclo*hepta*-1 : 3 : 6-*triene* (VIII).—The tropolone (VI; R = H) (120 mg.) was set aside overnight in methanol (15 ml.) containing sodium (11 mg.) and benzyl bromide (500 mg.). The solution was concentrated *in vacuo*, water added, and the suspension extracted with ethyl acetate. Concentration of the extract yielded an oil which was washed with petrol (b. p. 40—60°), and the residue crystallised from petrol (b. p. 60—80°), to give the *ether* (VI; R = CH_2Ph), m. p. 98—100° (Found: C, 71·25; H, 5·8. $C_{21}H_{20}O_5$ requires C, 71·6; H, 5·7%).

The ether was converted into the *oxime* (VIII), m. p. 171—172°, in the usual manner (Found: C, 68·8; H, 5·7; N, 4·0. $C_{21}H_{21}O_5N$ requires C, 68·65; H, 5·8; N, 3·8%). Light absorption in ethanol: $\lambda_{max.}$ (log ε) 255 (4·55), 288 (4·30), 337 mμ (3·72).

Microanalyses were carried out by Miss S. Watt and Mr. J. M. L. Cameron. The ultraviolet spectra were measured on a Unicam S.P. 500 spectrophotometer. One of us (J. K. S.) gratefully acknowledges a grant from D.S.I.R.

UNIVERSITY OF GLASGOW. [*Received, January 9th*, 1957.]

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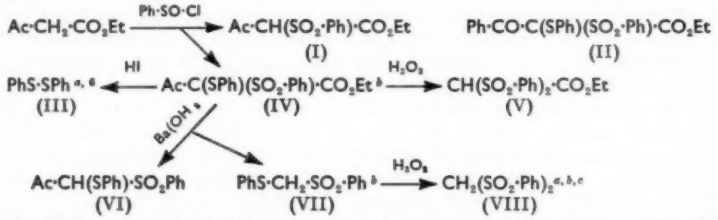
448. *Sulphonyl and Sulphinyl Derivatives of β-Keto-esters.*

By (Mrs.) E. M. Philbin, E. R. Stuart, R. F. Timoney, and T. S. Wheeler.

Ethyl *O*-methanesulphonylacetoacetate is rearranged by basic and acidic catalysts to the corresponding *C*-methylsulphonyl ester. Benzenesulphinyl chloride reacts with ethyl acetoacetate to give the *C*-sulphenylsulphonyl ester (IV), reactions of which are described. The benzoylacetate analogue of (IV) was similarly prepared.

Claisen and Haase [1] and Kästner [2] observed that ethyl (*O*-acyl)acylacetates rearranged in presence of acids or bases to the corresponding *C*-acyl esters. It has now been found that ethyl *O*-methanesulphonylacetoacetate undergoes a similar acid–base-catalysed rearrangement. Although ethyl *C*-benzylsulphonylacetoacetate, ethyl *C*-methylsulphonylbenzoylacetate, and ethyl *C*-benzylsulphonylbenzoylacetate were readily prepared, the corresponding *O*-derivatives could not be obtained. Arenesulphonyl halides do not condense with ethyl sodioacetoacetate.[3]

Condensation of benzenesulphinyl chloride with ethyl acetoacetate gave mainly ethyl α-phenylsulphenyl-α-phenylsulphonylacetoacetate (IV), and an oil which formed a cupro-derivative with analytical figures corresponding to the cupro-derivative of ethyl phenylsulphonylacetoacetate (I). Compound (II), the benzoylacetate analogue of (IV), was similarly prepared.



[a] Confirmed by m. p. with authentic samples: other numbered compounds are new. [b] SO_2 bands present in infrared spectrum (see Table). [c] Shriner, Struck, and Jorison, *J. Amer. Chem. Soc.*, 1930, **52**, 2060.

The structure of (IV) was established by its reactions (see diagram) and by infrared measurements (Table). The disproportionation of sulphinyl compounds to give sulphenylsulphonyl derivatives has been frequently discussed.[4] The production of diphenyl

Infrared spectra (cm.$^{-1}$) in chloroform.

Compound	SO_2 bands [12] 1160—1140 (s) and 1350—1300 (s)	SO bands [12] 1060—1040 (s)
(IV)	1142, 1150, 1309, 1321	
(VII)	1150, 1302, 1309	
(VIII) (authentic sample) [10]	1148, 1166, 1332, 1340	
$CH_2(SO{\cdot}Ph)_2$ (authentic sample) [11]		1043

disulphide (III) by the action of hydriodic acid on the ester (IV) adds to numerous instances of its formation in reactions in which the phenylsulphenyl group is present.[3, 5, 6]

[1] Claisen and Haase, *Ber.*, 1900, **33**, 3778; see Michael and Carlson, *J. Amer. Chem. Soc.*, 1935, **57**, 165.

[2] Kästner, Thesis, Marburg, 1937; "Newer Methods of Preparative Organic Chemistry," p. 289, Interscience Publ., Ltd., London, 1948.

[3] Kohler and MacDonald, *Amer. Chem. J.*, 1899, **22**, 227; Findeisen, *J. prakt. Chem.*, 1902, **65**, 529.

[4] See, for example Cymerman and Willis, *J.*, 1951, 1332; Kurzer, *J.*, 1953, 549; Houben-Weyl, "Methoden der Organischen Chemie," Georg Thieme Verlag, Stuttgart, 1955, Vol. IX, p. 687.

[5] See Miller and Smiles, *J.*, 1925, **127**, 224; Gibson, Miller, and Smiles, *ibid.*, p. 1821; Houben-Weyl, *op. cit.*, p. 55.

[6] Stenhouse, *Proc. Roy. Soc.*, 1868, **17**, 64, who gives m. p. 61°.

Gibson [7] considered that he had obtained compound (VI) by the condensation of phenylsulphonylacetone and *S*-phenylsulphonylthiophenol (phenyl benzenethiolsulphonate, $Ph{\cdot}SO_2{\cdot}SPh$) in presence of sodium ethoxide. His product has now been found to be compound (VII). The acetyl group in compound (VI) is readily removed by alkaline hydrolysis.

Experimental

Crystallisation was from ethanol unless otherwise stated.

Preparation of Sulphonylacylacetates.—Ethyl *C*-methylsulphonylacetoacetate (Found: C, 40·7; H, 6·1; S, 15·7. Calc. for $C_7H_{12}O_5S$: C, 40·4; H, 5·8; S, 15·4%) and ethyl *O*-methanesulphonylacetoacetate (Found: C, 40·1; H, 6·0; S, 14·8%. Calc. as for the *C*-derivative) were obtained as oils.[8] The *C*-ester gave a red colour with ferric chloride; the reaction of the *O*-ester was negative.

Ethyl C-*Benzylsulphonylacetoacetate.*—Toluene-ω-sulphonyl chloride (10 g.) and a suspension in ether (100 ml.) of ethyl sodioacetoacetate [from sodium (1·2 g.) and the ester (6·4 g.)] were refluxed together for 6 hr., and the resulting ethereal solution was extracted with ice-cold aqueous sodium hydroxide (7·5%) [giving extract (A)] and was washed with water and dried ($MgSO_4$). The light yellow oil obtained on evaporation of the solvent had b. p. 154—156°/1 mm. The analytical figures differed from those required for ethyl *O*-toluene-ω-sulphonylacetoacetate.

The alkaline extract, (A) above, on acidification yielded to ether a yellow-brown viscous oil, *ethyl* C-*benzylsulphonylacetoacetate*, b. p. 172—176°/1 mm. (distillate, 4·6 g.) (Found: C, 54·4; H, 5·6; S, 11·4. $C_{13}H_{16}O_5S$ requires C, 54·9; H, 5·7; S, 11·3%). The ethanolic ferric colour was red. The *cupro-derivative*, obtained when an ethereal solution of the *C*-benzylsulphonyl ester was shaken with aqueous cupric acetate, separated in blue prisms, m. p. 232—234° (Found: C, 49·3; H, 5·0; S, 10·6; Cu, 10·7. $C_{26}H_{30}O_{10}S_2Cu$ requires C, 49·6; H, 4·8; S, 10·2; Cu, 10·1%).

Repetition of Böhme and Fischer's experiment [8] confirmed that the interaction of ethyl sodiobenzoylacetate and methanesulphonyl chloride gives ethyl *C*-methylsulphonylbenzoylacetate (Found: C, 52·9; H, 5·1; S, 12·2. Calc. for $C_{12}H_{14}O_5S$: C, 53·3; H, 5·2; S, 11·8%) with no trace of the *O*-derivative.

Ethyl C-*Benzylsulphonylbenzoylacetate.*—This preparation was carried out as described for ethyl *C*-benzylsulphonylacetoacetate (above) using ethyl benzoylacetate (2·7 g.), sodium (0·3 g.), anhydrous ether (150 ml.) and toluene-ω-sulphonyl chloride (5 g.). The mixture was refluxed for 2 hr. The alkali-insoluble portion of the product gave analytical figures which did not correspond to those required for ethyl *O*-toluene-ω-sulphonylbenzoylacetate. The fraction soluble in alkali was *ethyl* C-*benzylsulphonylbenzoylacetate* (Found: C, 62·5; H, 5·5; S, 9·4. $C_{18}H_{18}O_5S$ requires C, 62·4; H, 5·2; S, 9·2%) which separated in plates (0·9 g.), m. p. 126—128°. The ethanolic ferric colour was red. The compound did not give a cupro-derivative. Böhme and Fischer [8] could not obtain a cupro-derivative from ethyl *C*-methylsulphonylbenzoylacetate which they showed existed mainly in the keto-form.

There was no evidence of formation of ethyl *O*-benzenesulphonylacetoacetate when ethyl acetoacetate and benzenesulphonyl chloride were heated in presence of pyridine at 150° for 1 hr. Similar negative results were obtained when the pyridine–acid chloride method was applied under a variety of conditions to prepare ethyl *O*-toluene-ω-sulphonylacetoacetate and ethyl *O*-methanesulphonylbenzoylacetate.

Transformation of Ethyl O-*Methanesulphonylacetoacetate into the Corresponding* C-*Derivative.*—(*a*) A mixture of ethyl *O*-methanesulphonylacetoacetate (0·6 g.), dry pyridine (10 ml.), and hot-powdered sodium hydroxide (0·5 g.) was shaken at room temperature for 12 hr. and acidified. The ethereal extract of the product was washed with ice-cold aqueous sodium hydroxide (7·5%), and the alkaline solution was acidified and extracted with ether. The oil (0·3 g.) which remained on evaporation of the solvent was ethyl *C*-methylsulphonylacetoacetate. It gave a red colour with ethanolic ferric chloride and with phenylhydrazine yielded *N*-acetyl-*N'*-phenylhydrazine (Found: N, 18·3. Calc. for $C_8H_{10}ON_2$: N, 18·7%), m. p. 124—126°, not depressed by addition of samples of similar m. p., prepared from authentic ethyl *C*-methylsulphonylacetoacetate,[8] and from phenylhydrazine and acetic anhydride.[9]

[7] Gibson, *J.*, 1932, 1824.
[8] Böhme and Fischer, *Ber.*, 1943, **76**, 92.
[9] Fischer, *Annalen*, 1878, **190**, 129.

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(*b*) When in the above experiment sodium hydroxide was replaced by potassium cyanide, and the mixture was heated at the b. p. of pyridine for 2 hr., the yield of *C*-methylsulphonyl ester was 15%.

(*c*) Boron trifluoride was passed through an anhydrous ethereal solution (5%) of ethyl *O*-methanesulphonylacetoacetate until absorption was complete (40 min.). The product was shaken with 30% aqueous sodium acetate, and the ethereal solution was washed with aqueous sodium hydrogen carbonate and with water, and dried ($MgSO_4$). Evaporation of the solvent gave ethyl *C*-methylsulphonylacetoacetate (30% yield) which was identified as described at (*a*).

Reaction of Benzenesulphinyl Chloride with Ethyl Acetoacetate.—The chloride (12 g.) was added dropwise to a mixture of ethyl acetoacetate (6·5 g.) and pyridine (8 g.) at 0° and the product extracted with ether after 12 hr. The ethereal solution was washed with dilute acid and alkali. Removal of the solvent gave *ethyl α-phenylsulphenyl-α-phenylsulphonylacetoacetate* (IV), which crystallised in prisms (11·7 g.), m. p. 83—84° (Found : C, 56·9; H, 4·6; S, 16·8. $C_{18}H_{18}O_5S_2$ requires C, 57·1; H, 4·8; S, 16·9%).

Acidification of the alkaline extract of the ethereal solution yielded a yellowish-brown oil (1·1 g.) which could not be distilled. The *cupro-derivative*, which separated in blue-green needles, m. p. 242—243°, gave analytical figures corresponding to ethyl cuprophenylsulphonylacetoacetate (cf. I) (Found : C, 48·2; H, 4·4; S, 10·0; Cu, 10·0. $C_{24}H_{26}O_{10}S_2Cu$ requires C, 47·9; H, 4·3; S, 10·6; Cu, 10·5%).

Ethyl α-phenylsulphenyl-α-phenylsulphonylbenzoylacetate (II) was prepared similarly to compound (IV) from benzenesulphinyl chloride (12 g.), ethyl benzoylacetate (9·6 g.), and pyridine (8·4 g.). The product separated in needles (19·6 g.), m. p. 157—158° (Found : C, 62·7; H, 4·5; S, 14·4. $C_{23}H_{20}O_5S_2$ requires C, 62·7; H, 4·5; S, 14·5%).

Reactions of Ester (IV).—Since the ester remained unchanged when refluxed with water for 1 hr., 0·5N-barium hydroxide was employed. The liquid after filtration was extracted with ether. Evaporation of the solvent gave an oil which was diluted with ethanol and kept at 0° for 24 hr. Two solids, (VI) and (VII), separated in succession. *1-Phenylsulphenyl-1-phenylsulphonylacetone* (VI) crystallised in needles (0·4 g.), m. p. 110—111° (Found : C, 59·3; H, 4·6; S, 21·0. $C_{15}H_{14}O_3S_2$ requires C, 58·8; H, 4·6; S, 20·9%). *α-Phenylsulphenyl-α-phenylsulphonylmethane* (VII) separated in needles (0·9 g.), m. p. 61—62° (Found : C, 59·3; H, 4·4; S, 24·2. $C_{13}H_{12}O_2S_2$ requires C, 59·1; H, 4·6; S, 24·2%). Compound (VII) was also obtained (mixed m. p.) by condensation of phenylsulphonylacetone with phenyl benzenethiolsulphonate by Gibson's method [7] [product said to be (VI)], being indistinguishable from (VII) by analysis for carbon and hydrogen.

A mixture of the ester (IV) (2 g.), hydrogen peroxide (4 ml.; 100-vol.), acetic anhydride (10 ml.), and acetic acid (30 ml.) was, after two days, diluted with water, and kept at 0° for 12 hr. The resulting *ethyl di(phenylsulphonyl)acetate* (V) crystallised in needles (0·5 g.), m. p. 134—135° (Found : C, 52·3; H, 4·4; S, 17·1. $C_{16}H_{16}O_6S_2$ requires C, 52·2; H, 4·4; S, 17·4%). Hydrolysis of this ester (V) by boiling 20% aqueous sodium hydroxide for 1½ hr. gave di(phenylsulphonyl)methane [10] (VIII), m. p. and mixed m. p. 117—118° (Found : C, 52·9; H, 4·2; S, 21·9. Calc. for $C_{13}H_{12}O_4S_2$: C, 52·7; H, 4·1; S, 21·6%).

The ester (IV) (1 g.), hydriodic acid (3 ml.; *d* 1·7), and acetic anhydride (6 ml.) were heated on a steam-bath for 30 min., then added to aqueous sodium hydrogen sulphite. The resulting solid crystallised from aqueous ethanol in needles, m. p. and mixed m. p. with diphenyl disulphide [6] (III) 59—60°.

Reactions of α-Phenylsulphenyl-α-phenylsulphonylmethane (VII).—Oxidation of this compound by hydrogen peroxide in glacial acetic acid (see above) gave di(phenylsulphonyl)methane (VIII) (mixed m. p.).[10] Attempts to reduce compound (VII) by zinc dust and acetic acid at the b. p. or by hydriodic acid and acetic anhydride at 150—160° for 45 min. were unsuccessful. On the other hand, both di(phenylsulphinyl)methane [11] and α-phenylsulphinyl-α-phenylsulphonylmethane [11] were reduced to di(phenylsulphenyl)methane [10] by treatment with hydriodic acid and acetic anhydride at room temperature.

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[10] Shriner, Struck, and Jorison, *J. Amer. Chem. Soc.*, 1930, **52**, 2060.
[11] Hinsberg, *J. prakt. Chem.*, 1912, **85**, 337.
[12] Bellamy, "The Infrared Spectra of Complex Molecules," Chapter 22, Methuen & Co., Ltd., London, 1954.

449. *A Molecular Theory of the Electro-optical Kerr Effect in Liquids.*

By A. D. Buckingham and R. E. Raab.

The classical statistical-mechanical theory of the electro-optical Kerr constant is extended to include the effects of molecular interactions and of the dependence of molecular polarizabilities on field strength. The resulting formula is simple for molecules without permanent dipole moments for which it is found that at all densities the molecular Kerr constant is expressible in the form $A + B/T$, where A and B are constants characteristic of the substance. Experiments suggest that at room temperature A is responsible for about half of the observed Kerr constant of mesitylene. For pure polar liquids, the Kerr constant reduces to an expression involving, *inter al.*, the static and high-frequency dielectric constants. The final equation depends only on short-range effects, and for the Onsager model of a pure polar liquid leads to a simple result which agrees quite well with experimental data. The general result is applied to water, and Pople's molecular model used to compute the temperature dependence of its Kerr constant.

The Langevin–Born theory of the electro-optical Kerr effect (double refraction induced in an isotropic medium by an electric field) was recently extended [1] to include contributions resulting from the dependence of molecular polarizability on field strength. For spherically symmetric molecules the observed Kerr constant is independent of temperature and directly proportional to the " hyperpolarizability " describing the initial deviation from a linear relation between dipole moment and field strength. However, this extended Langevin–Born theory is strictly applicable only to perfect gases, whereas most of the existing data refer to solutions or pure liquids.

Earlier attempts [2] to extend the simple-gas theory to assemblies of interacting molecules have depended on assumptions inherent in various models. Recently a classical statistical-mechanical theory was developed and this has been applied successfully to non-dipolar substances [3] and to dilute solutions of polar molecules in non-polar solvents.[4] The present paper aims to interpret observed Kerr constants, particularly those of pure polar liquids, in terms of molecular properties. The general theory leads to an expression relating the constant to the anisotropy in the polarizability and to the mean values of the scalar products of vectors involving the mean dipole moments of a fixed molecule and its near neighbours. The effects of molecular interactions are in part allowed for by relating the Kerr constant to the actual dielectric constant of the medium.

General Theory

The molecular Kerr constant ${}_{\mathrm{m}}K$ as defined by Otterbein [5] is

$$ {}_{\mathrm{m}}K = \frac{6nV_{\mathrm{m}}}{(n^2+2)^2(\varepsilon+2)^2} \lim_{E\to 0} \frac{n_{\parallel}-n_{\perp}}{E^2} \quad . \quad . \quad . \quad . \quad . \quad . \quad (1) $$

where $n_{\parallel}$ and $n_{\perp}$ are the refractive indices of the specimen in the directions of the strong static electric field E and at right angles to it, and n is the refractive index of the isotropic medium for the same wavelength; V_{m} is the molar volume and ε the static dielectric constant. Our discussion will be restricted to systems in which the strong electric field E is uniform.

[1] Buckingham and Pople, *Proc. Phys. Soc.*, 1955, **68**, *A*, 905.
[2] Raman and Krishnan, *Proc. Roy. Soc.*, 1927, *A*, **117**, 1; Oka, *Proc. Phys.-Math. Soc. Japan* (3), **19**, 156; Piekara, *Proc. Roy. Soc.*, 1939, *A*, **172**, 360; Klages, *Z. Naturforsch.*, 1952, **7a**, 669.
[3] Buckingham, *Proc. Phys. Soc.*, 1955, **68**, *A*, 910.
[4] Buckingham, *Trans. Faraday Soc.*, 1956, **52**, 611.
[5] Otterbein, *Physikal. Z.*, 1934, **35**, 249.

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In order to isolate the "external" electric field E_0 as the effective macroscopic local field acting on a molecule, we shall consider a large spherical specimen of volume V_m containing N (Avogadro's number) similar molecules. If E_0 is the strength of the uniform field at large distances from the sphere, then classical electrostatics leads to the result $E = 3E_0/(\varepsilon + 2)$ (see Stratton [6]), and eqn. (1) becomes

$$ {}_mK = \frac{2nV_m}{3(n^2+2)^2} \lim_{E_0 \to 0} \frac{n_\parallel - n_\perp}{{E_0}^2} \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (2) $$

We shall suppose that the dipole moment $m_\alpha^{(i)}$ of the i-th molecule can be developed as a power series in the electric field acting on it. Thus, small Greek letters being used as tensor suffixes:

$$ m_\alpha^{(i)} = \mu_\alpha^{(i)} + \alpha_{\alpha\beta}^{(i)} (E_{0\beta} + F_\beta^{(i)}) + \tfrac{1}{2} \beta_{\alpha\beta\gamma}^{(i)} (E_{0\beta} + F_\beta^{(i)})(E_{0\gamma} + F_\gamma^{(i)}) + $$
$$ (1/6)\gamma_{\alpha\beta\gamma\delta}^{(i)}(E_{0\beta} + F_\beta^{(i)})(E_{0\gamma} + F_\gamma^{(i)})(E_{0\delta} + F_\delta^{(i)}) + \quad . \quad . \quad (3) $$

where $\mu_\alpha^{(i)}$ is the permanent dipole moment of molecule i; $\alpha_{\alpha\beta}^{(i)}$, $\beta_{\alpha\beta\gamma}^{(i)}$, $\gamma_{\alpha\beta\gamma\delta}^{(i)}$, etc., are the polarizability tensors discussed by Buckingham and Pople; [1] these are symmetric in all suffixes. $\alpha_{\alpha\beta}^{(i)}$ is the normal low-field strength polarizability tensor, and $\beta_{\alpha\beta\gamma}^{(i)}$, $\gamma_{\alpha\beta\gamma\delta}^{(i)}$, etc., describe the field dependence of the polarizability. $F_\alpha^{(i)}$ is the field at the centre of molecule i due to the charge distributions of all of the others, and we shall assume that $F_\alpha^{(i)}$ is constant throughout the molecule. The dipolar contribution to $F_\alpha^{(i)}$ is

$$ F_\alpha^{(i)} = -\sum_{j \neq i}^{N} \varepsilon_{\alpha\beta}^{(ij)} m_\beta^{(j)} $$
$$ = -\sum_{j \neq i}^{N} \frac{1}{r_{ij}^5} (r_{ij}^2 \delta_{\alpha\beta} - 3r_{ij\alpha}r_{ij\beta}) m_\beta^{(j)} \quad . \quad . \quad . \quad . \quad . \quad . \quad (4) $$

$r_{ij\alpha}$ being the vector between the centres of molecules i and j, and $\delta_{\alpha\beta}$ the substitution tensor ($= 1$ when $\alpha = \beta$; $= 0$ when $\alpha \neq \beta$).

The *differential polarizability* $\pi_{\alpha\epsilon}^{(i)}$ of molecule i is defined as

$$ \pi_{\alpha\epsilon}^{(i)} = \frac{\partial m_\alpha^{(i)}}{\partial E_{0\epsilon}} = \pi_{\epsilon\alpha}^{(i)} \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (5) $$

$$ = \{\alpha_{\alpha\beta}^{(i)} + \beta_{\alpha\beta\gamma}^{(i)}(E_{0\gamma} + F_\gamma^{(i)}) + \tfrac{1}{2}\gamma_{\alpha\beta\gamma\delta}^{(i)}(E_{0\gamma} + $$
$$ F_\gamma^{(i)})(E_{0\delta} + F_\delta^{(i)}) + \ldots\}\{\delta_{\beta\epsilon} + \partial F_\beta^{(i)}/\partial E_{0\epsilon}\}. \quad . \quad (6) $$

The effective molecular polarizability determining the refractivities in the directions of the unit vectors $\mathbf{e}^\parallel$ and $\mathbf{e}^\perp$ along and at right angles respectively to the strong field $\mathbf{E}_0$ is $\pi_{\alpha\beta}^{(i)}$, for they are proportional to the mean dipole moments induced in these directions by the incremental high-frequency electric fields of the light waves. Thus

$$ \frac{{n_\parallel}^2 - 1}{{n_\parallel}^2 + 2} - \frac{{n_\perp}^2 - 1}{{n_\perp}^2 + 2} = \frac{4\pi N}{3V_m} \overline{\Pi^{(1)}(\tau, \mathbf{E}_0)} \quad . \quad . \quad . \quad . \quad . \quad . \quad (7) $$

where

$$ \Pi^{(1)}(\tau, \mathbf{E}_0) = \pi_{\alpha\beta}^{(1)} (e_\alpha^\parallel e_\beta^\parallel - e_\alpha^\perp e_\beta^\perp) \quad . \quad . \quad . \quad . \quad . \quad . \quad (8) $$

In our purely classical treatment, the continuous variable τ represents the configuration of

[6] Stratton, "Electromagnetic Theory," McGraw-Hill Book Co., New York, 1941, § 3.24.

the molecules of the specimen. The bar in eqn. (7) signifies an average over all configurations, so that

$$\overline{\Pi^{(1)}(\tau, \mathbf{E}_0)} = \frac{\int \Pi^{(1)}(\tau, \mathbf{E}_0) \exp\{-U(\tau, \mathbf{E}_0)/\boldsymbol{kT}\}\mathrm{d}\tau}{\int \exp\{-U(\tau, \mathbf{E}_0)/\boldsymbol{kT}\}\mathrm{d}\tau} \quad . \quad . \quad . \quad . \quad (9)$$

where $U(\tau, \mathbf{E}_0)$ is the potential energy of the system in the configuration τ and when the external field is $\mathbf{E}_0$. The general relation

$$U(\tau, \mathbf{E}_0) = U(\tau, 0) - \int_0^{E_0} M_\alpha(\tau, \mathbf{E})\, e_\alpha^{\parallel}\, \mathrm{d}E \quad . \quad . \quad . \quad . \quad . \quad (10)$$

leads to the result

$$\partial U(\tau, \mathbf{E}_0)/\partial E_0 = -M_\alpha(\tau, \mathbf{E}_0) e_\alpha^{\parallel} \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (11)$$

where $M_\alpha(\tau, \mathbf{E}) = \sum_i^N m_\alpha^{(i)}$ is the dipole moment of the whole spherical specimen when the external field is $\mathbf{E}$.

We shall employ the notation $\langle X \rangle$ for the average value of a quantity $X(\tau, \mathbf{E}_0)$ in the assembly with $E_0 = 0$, that is,

$$\langle X \rangle = \frac{\int X(\tau, 0) \exp\{-U(\tau, 0)/\boldsymbol{kT}\}\mathrm{d}\tau}{\int \exp\{-U(\tau, 0)/\boldsymbol{kT}\}\mathrm{d}\tau} \quad . \quad . \quad . \quad . \quad . \quad (12)$$

From eqns. (2) and (7)

$${}_mK = \frac{2\pi \boldsymbol{N}}{27}\left(\frac{\partial^2 \overline{\Pi^{(1)}(\tau, \mathbf{E}_0)}}{\partial {E_0}^2}\right)_{E_0 = 0} \quad . \quad . \quad . \quad . \quad . \quad . \quad (13)$$

which with eqn. (9) leads to

$${}_mK = \frac{2\pi \boldsymbol{N}}{27}\left\langle \frac{\partial^2 \Pi^{(1)}}{\partial {E_0}^2} - \frac{1}{\boldsymbol{kT}}\left(2\frac{\partial \Pi^{(1)}}{\partial E_0}\frac{\partial U}{\partial E_0} + \Pi^{(1)}\frac{\partial^2 U}{\partial {E_0}^2}\right) + \frac{1}{\boldsymbol{k^2T^2}}\Pi^{(1)}\left(\frac{\partial U}{\partial E_0}\right)^2 \right\rangle \quad (14)$$

whence, through eqn. (8),

$${}_mK = \frac{2\pi \boldsymbol{N}}{27}\left\langle \left\{ \frac{\partial^2 \pi_{\alpha\beta}^{(1)}}{\partial E_{0\gamma}\partial E_{0\delta}} + \frac{1}{\boldsymbol{kT}}\left(2\frac{\partial \pi_{\alpha\beta}^{(1)}}{\partial E_{0\gamma}} M_\delta + \Pi_{\alpha\beta}^{(1)}\frac{\partial M_\gamma}{\partial E_{0\delta}}\right) + \frac{1}{\boldsymbol{k^2T^2}}\pi_{\alpha\beta}^{(1)} M_\gamma M_\delta \right\}\left\{ e_\gamma^{\parallel} e_\delta^{\parallel}(e_\alpha^{\parallel} e_\beta^{\parallel} - e_\alpha^{\perp} e_\beta^{\perp}) \right\} \right\rangle \quad . \quad (15)$$

In averaging (15), we shall use the result [1] that when all directions of $\mathbf{e}^{\parallel}$ are equally likely (as when E_0 is zero)

$$\left\langle e_\gamma^{\parallel} e_\delta^{\parallel}(e_\alpha^{\parallel} e_\beta^{\parallel} - e_\alpha^{\perp} e_\beta^{\perp}) \right\rangle = (1/30)\{-2\delta_{\alpha\beta}\delta_{\gamma\delta} + 3\delta_{\alpha\gamma}\delta_{\beta\delta} + 3\delta_{\alpha\delta}\delta_{\beta\gamma}\} \quad . \quad . \quad (16)$$

so that (15) becomes

$${}_mK = \frac{2\pi \boldsymbol{N}}{405}\left\langle 2\frac{\partial^3 m_\alpha^{(1)}}{\partial E_{0\alpha}\partial E_{0\beta}\partial E_{0\beta}} + \frac{4}{\boldsymbol{kT}}\frac{\partial^2 m_\alpha^{(1)}}{\partial E_{0\alpha}\partial E_{0\beta}} M_\beta + \frac{1}{\boldsymbol{kT}}\left\{ 3\pi_{\alpha\beta}^{(1)}\frac{\partial M_\alpha}{\partial E_{0\beta}} - \pi_{\alpha\alpha}^{(1)}\frac{\partial M_\beta}{\partial E_{0\beta}} \right\} + \frac{1}{\boldsymbol{k^2T^2}}\left\{ 3\pi_{\alpha\beta}^{(1)} M_\alpha M_\beta - \pi_{\alpha\alpha}^{(1)} M_\beta M_\beta \right\} \right\rangle \quad (17)$$

Eqn. (17) is the complete classical statistical-mechanical formula for ${}_mK$ and is the generalization of the perfect-gas result of Buckingham and Pople.[1]

Theory for the microscopic scale.

(a) *Non-polar Substances.*—For molecules with centres of inversion, μ_α and $\beta_{\alpha\beta\gamma}$ are zero, and to a good approximation eqn. (17) reduces to

$$ {}_mK = \frac{2\pi N}{405}\left[2\gamma_{\alpha\alpha\beta\beta}^{(1)} + \frac{1}{kT}\sum_i^N \left\langle 3\alpha_{\alpha\beta}^{(1)}\alpha_{\alpha\beta}^{(0)(i)} - \alpha_{\alpha\alpha}^{(1)}\alpha_{\beta\beta}^{(0)(i)}\right\rangle\right] \quad . \quad . \quad (18) $$

where $\alpha^{(1)}$ and $\gamma^{(1)}$ are polarizabilities for the frequency of the incident light, and $\alpha^{(0)}$ is a static field value; $\alpha^{(0)}$ may differ from α because of dispersion effects and atomic polarization. However, the frequency dependence of ${}_mK$ is normally very small. In eqn. (18) terms in the cube of α and in $\alpha\gamma$ have been omitted, but these are normally unimportant. It has been shown [3] that eqn. (18) can be written in terms of the mean polarizabilities $\alpha = \frac{1}{3}\alpha_{\alpha\alpha}$ and $\alpha^{(0)}$ in the form

$$ {}_mK = \frac{2\pi N}{405}\left[2\gamma_{\alpha\alpha\beta\beta}^{(1)} + \frac{3}{kT}\left\{\sum_{s=1}^{3}\alpha_s\alpha_s^{(0)} - 3\alpha\alpha^{(0)} + \sum_{s,t=1}^{3}\alpha_s\alpha_t^{(0)}\iint(\cos^2\theta_{st} - \tfrac{1}{3})n_2(\mathbf{r},\omega)\mathrm{d}\mathbf{r}\mathrm{d}\omega\right\}\right] \quad . \quad . \quad (19) $$

where α_s and $\alpha_s^{(0)}$ are principal polarizabilities of a molecule in the oscillating and static fields, θ_{st} is the angle between the s-principal axis of molecule 1 and the t-principal axis of another molecule whose position and orientation are represented by $(\mathbf{r}, \omega)$ relative to molecule 1 fixed at the origin, and where $n_2(\mathbf{r}, \omega)\mathrm{d}\mathbf{r}\mathrm{d}\omega$ is the probability of there being a molecule in the volume element $\mathrm{d}\mathbf{r}$ and orientational element $\mathrm{d}\omega$. For dipolar forces, the integral in eqn. (19) converges rapidly, there being no long-range contribution to $\langle\cos^2\theta_{st} - \frac{1}{3}\rangle$.

It is shown on p. 2350 that the integral in eqn. (19) is only about 0·001 for water, so that it is quite unimportant in this case. $\langle\cos^2\theta - \frac{1}{3}\rangle$ is in principle measurable through light-scattering experiments,[7] or through observations of magnetic double refraction,[8] but we shall assume that its contribution to ${}_mK$ is negligible. Thus

$$ {}_mK = A + B/T = \frac{2\pi N}{405}\left[2\gamma_{\alpha\alpha\beta\beta}^{(1)} + \frac{3}{kT}\left(\sum_{s=1}^{3}\alpha_s\alpha_s^{(0)} - 3\alpha\alpha^{(0)}\right)\right] \quad . \quad . \quad (20) $$

where A and B are molecular constants. Equation (20) is the perfect-gas result, so that ${}_mK$ for non-polar molecules should be nearly independent of density; this result was deduced earlier, and observations of the Kerr constants of non-polar substances over wide pressure ranges support the conclusion.[3]

The Langevin equation,[9] ${}_mK = B/T$, omits the induced anisotropy term (the one in γ); as many of the principal polarizabilities α_s quoted in the literature are derived from this incomplete equation, they must be viewed with reservation until the importance of the γ term has been experimentally determined for a variety of substances. The magnitude of this term in the case of carbon disulphide may be obtained from Lyon and Wolfram's observations [10] of the temperature dependence of ${}_mK$ in the liquid. The plot of ${}_mK$ against $1/T$ shows that the γ term, obtained by extrapolation to $1/T = 0$, contributes about one quarter of the room-temperature value of ${}_mK$ (see Figure). Again, the temperature dependence of ${}_mK$ for mesitylene, measured by Grodde,[11] shows that the γ term is responsible for approximately one half of the observed ${}_mK$ at room temperature.

[7] Benoit and Stockmayer, *J. Phys. Radium*, 1956, **17**, 21.
[8] Buckingham and Pople, *Proc. Phys. Soc.*, 1956, **69**, *B*, 1133.
[9] Langevin, *Le Radium*, 1910, **7**, 249.
[10] Lyon and Wolfram, *Ann. Physik*, 1920, **63**, 739.
[11] Grodde, *Physikal. Z.*, 1938, **39**, 772.

In applying eqn. (20) we shall, following Le Fèvre and Le Fèvre,[12] take $\alpha_s^{(0)}/\alpha_s = {}_DP/{}_EP$ where ${}_DP$ and ${}_EP$ are the distortion and electronic polarizations respectively (this assumption may sometimes be doubtful [4]). α is evaluated from $4\pi N\alpha/3 = {}_EP$.

For molecules that are symmetric about the 1-axis, eqn. (20) becomes

$$ {}_mK = \frac{2\pi N}{405}\left[2\gamma_{\alpha\alpha\beta\beta} + \frac{9}{2kT}\frac{{}_DP}{{}_EP}(\alpha_1 - \alpha)^2\right] \quad . \quad . \quad . \quad . \quad . \quad (21)$$

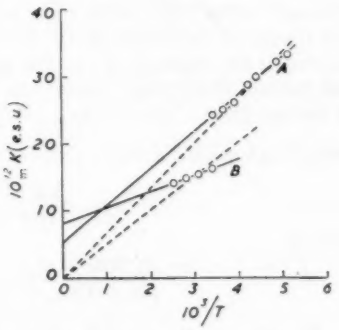
The results of calculations on data for carbon disulphide and mesitylene are shown in Table 1.

TABLE 1. *Principal polarizabilities.*

	Carbon disulphide			Mesitylene		
Principal polarizabilities	Calc. with ${}_mK = A + B/T$	Calc. with ${}_mK = B/T$	Previous values	Calc. with ${}_mK = A + B/T$	Calc. with ${}_mK = B/T$	Previous values
$10^{24}\alpha_1$ (cm.^{3})	12·1	12·5	13·9 [a]	12·8	11·6	12·5 [b]
$10^{24}\alpha_2 = \alpha_3$ (cm.^{3})	6·04	5·83	5·10 [a]	16·9	17·5	17·0 [b]
$10^{36}\gamma = 10^{36}\gamma_{\alpha\beta\beta\beta}/5$ (e.s.u.)	54·4	0	—	85·2	0	—

[a] Landolt–Börnstein Tabellen, 1951, **3**, 514, 515. [b] Le Fèvre and Le Fèvre, *Rev. Pure Appl. Chem.* (*Australia*), 1955, **5**, 261.

We have used, for carbon disulphide, ${}_DP = 22{\cdot}7$ cm.^{3} and ${}_EP = 20{\cdot}3$ cm.^{3}, and, for mesitylene, ${}_DP = 41{\cdot}4$ cm.^{3} and ${}_EP = 39{\cdot}2$ cm.^{3} (ref. *a*, Table 1).



A, Carbon disulphide.
B, Mesitylene.
Broken and full lines relate respectively to the exclusion and inclusion of the temperature-independent contribution to m*K*.

The agreement between the α_s values of Le Fèvre and Le Fèvre (ref. *b*, Table 1) and those found by us for mesitylene, using Grodde's data,[11] may be fortuitous, since the former were obtained through the application of the Langevin equation to dilute-solution measurements. However, γ should be as important in solutions as in a gas or pure liquid.

It may be noted that the graphs of ${}_mK$ against $1/T$ for carbon disulphide and mesitylene are approximately linear, providing further justification for our neglect of $\langle\cos^2\theta - \frac{1}{3}\rangle$ in the derivation of eqn. (20).

(b) *Polar Substances.*—For polar substances, the final term in eqn. (17) will be important; in it we shall approximate $\pi_{\alpha\beta}$ by $\alpha_{\alpha\beta}$. By expressing $\alpha_{\alpha\beta}$ in terms of the principal components α_1, α_2, α_3 we find

$$\left\langle 3\alpha_{\alpha\beta}^{(1)}M_\alpha M_\beta - \alpha_{\alpha\alpha}^{(1)}M^2 \right\rangle = 3\left\langle \sum_{s=1}^{3}\alpha_s M_s^2 - \alpha M^2 \right\rangle \quad . \quad . \quad . \quad (22)$$

If the molecule is symmetric about the 1-axis, then $\langle M_2^2\rangle = \langle M_3^2\rangle$; we shall suppose that this relation is also true for assemblies of molecules whose permanent moments lie

[12] Le Fèvre and Le Fèvre, *J.*, 1953, 4041.

along the principal axes of their polarizability ellipsoids, despite the possibility that α_2 may not be equal to α_3. Thus

$$\left\langle \sum_{s=1}^{3} \alpha_s M_s^2 - \alpha M^2 \right\rangle = (3/2)(\alpha_1 - \alpha)\left\langle M_1^2 - \tfrac{1}{3}M^2 \right\rangle = (3/2)(\alpha_1 - \alpha)f \qquad (23)$$

We shall evaluate f $(= \langle M_1^2 - \frac{1}{3}M^2 \rangle)$ by putting $\mathsf{M} = \sum_i \mathsf{m}^{(i)}$ and $M_1 = (1/\mu)\sum_i \boldsymbol{\mu}^{(1)} \cdot \mathsf{m}^{(i)}$. Thus

$$f = \frac{1}{\mu^2}\sum_i{}' \left\langle \boldsymbol{\mu}^{(1)} \cdot \mathsf{m}^{(i)} \boldsymbol{\mu}^{(1)} \cdot \mathsf{M} - \tfrac{1}{3}\mu^2 \mathsf{m}^{(i)} \cdot \mathsf{M} \right\rangle + \frac{1}{\mu^2}\sum_j{}'' \left\langle \boldsymbol{\mu}^{(1)} \cdot \mathsf{m}^{(j)} \boldsymbol{\mu}^{(1)} \cdot \mathsf{M} - \tfrac{1}{3}\mu^2 \mathsf{m}^{(j)} \cdot \mathsf{M} \right\rangle \qquad (24)$$

where Σ' is a summation over molecule i and all those in short-range interaction with it (that is, those within a small macroscopic sphere centred on molecule 1), and Σ'' implies a sum over the remainder of the molecules. On writing $\mathsf{m}^{(i)} = \boldsymbol{\mu}^{(i)} + \mathsf{m}'^{(i)}$ and $\mathsf{M}' = \sum_i \mathsf{m}'^{(i)}$, and neglecting terms proportional to $(m')^2$ [that is, those of $0(\alpha^2)$], we obtain from eqn. (24)

$$f = \tfrac{2}{3}\left\langle \boldsymbol{\mu}^{(1)} \cdot (\mathsf{M} + \mathsf{M}') \right\rangle + \frac{1}{\mu^2}\sum_{i \neq 1}{}' \left\langle \left\{ \boldsymbol{\mu}^{(1)} \cdot \boldsymbol{\mu}^{(i)} \boldsymbol{\mu}^{(1)} - \tfrac{1}{3}\mu^2 \boldsymbol{\mu}^{(i)} \right\} \cdot \left\{ \mathsf{M} + \mathsf{M}' \right\} \right\rangle$$
$$+ \frac{1}{\mu^2}\sum_j{}'' \left\langle \left\{ \boldsymbol{\mu}^{(1)} \cdot \boldsymbol{\mu}^{(j)} \boldsymbol{\mu}^{(1)} - \tfrac{1}{3}\mu^2 \boldsymbol{\mu}^{(j)} \right\} \cdot \left\{ \mathsf{M} + \mathsf{M}' \right\} \right\rangle \quad . \qquad (25)$$

To evaluate $\langle \boldsymbol{\mu}^{(1)} \cdot (\mathsf{M} + \mathsf{M}') \rangle$ we must know the mean value of $(\mathsf{M} + \mathsf{M}')$ when $\boldsymbol{\mu}^{(1)}$ is fixed, and, for terms of the type $\langle (\boldsymbol{\mu}^{(1)} \cdot \boldsymbol{\mu}^{(i)})(\boldsymbol{\mu}^{(1)} \cdot (\mathsf{M} + \mathsf{M}')) \rangle$, the mean value of $(\mathsf{M} + \mathsf{M}')$ when $\boldsymbol{\mu}^{(1)}$ and $\boldsymbol{\mu}^{(i)}$ are fixed. The problems involved are similar to those found in the general theory of the static dielectric constant ε, where $\langle \boldsymbol{\mu}^{(1)} \cdot (\mathsf{M} + \mathsf{M}') \rangle$ occurs.[13] The essential step is the replacement of the medium outside a sphere enclosing the fixed molecules and those in short-range interaction with them, by a continuum having the bulk properties of the specimen. Then, if $\mathsf{m}_{\text{av.}}$ $(= (\sum_i{}' \mathsf{m}^{(i)})_{\text{av.}})$ is the mean dipole moment of this small macroscopic sphere, the average value of M is given by

$$\frac{9\varepsilon}{(2\varepsilon + 1)(\varepsilon + 2)}\,\mathsf{m}_{\text{av.}}$$

and that of M' by

$$\frac{3(2\varepsilon + \varepsilon_\infty)}{(2\varepsilon + 1)(\varepsilon_\infty + 2)}\,\mathsf{m}_{\text{av.}} - \boldsymbol{\mu}_{\text{av.}}$$

where $\boldsymbol{\mu}_{\text{av.}}$ $(= (\sum_i{}' \boldsymbol{\mu}^{(i)})_{\text{av.}})$ is the mean "permanent" moment of the small sphere, and ε_∞ the high-frequency dielectric constant. Thus the mean of $(\mathsf{M} + \mathsf{M}')$ is

$$(\mathsf{M} + \mathsf{M}')_{\text{av.}} = \frac{6(\varepsilon^2 + 5\varepsilon + 2\varepsilon\varepsilon_\infty + \varepsilon_\infty)}{(2\varepsilon + 1)(\varepsilon + 2)(\varepsilon_\infty + 2)}\,\mathsf{m}_{\text{av.}} - \boldsymbol{\mu}_{\text{av.}} \quad . \quad . \quad . \quad . \qquad (26)$$

With this result, the complete formula for f becomes

$$f = \tfrac{2}{3}\left[\frac{6(\varepsilon^2 + 5\varepsilon + 2\varepsilon\varepsilon_\infty + \varepsilon_\infty)}{(2\varepsilon + 1)(\varepsilon + 2)(\varepsilon_\infty + 2)}\,\boldsymbol{\mu} \cdot \bar{\mathsf{m}} - \boldsymbol{\mu} \cdot \bar{\boldsymbol{\mu}} \right] + \frac{1}{\mu^2}\sum_{i \neq 1}{}' \left\langle \left\{ \boldsymbol{\mu}^{(1)} \cdot \boldsymbol{\mu}^{(i)} \boldsymbol{\mu}^{(1)} \right.\right.$$
$$\left. - \tfrac{1}{3}\mu^2 \boldsymbol{\mu}^{(i)} \right\} \cdot \left\{ \frac{6(\varepsilon^2 + 5\varepsilon + 2\varepsilon\varepsilon_\infty + \varepsilon_\infty)}{(2\varepsilon + 1)(\varepsilon + 2)(\varepsilon_\infty + 2)}\,\bar{\bar{\mathsf{m}}}^{(1i)} - \bar{\bar{\boldsymbol{\mu}}}^{(1i)} \right\} \Big\rangle + \frac{1}{\mu^2}\sum_j{}'' \left\langle \left\{ \boldsymbol{\mu}^{(1)} \cdot \boldsymbol{\mu}^{(j)} \boldsymbol{\mu}^{(1)} \right.\right.$$
$$\left. \left. - \tfrac{1}{3}\mu^2 \boldsymbol{\mu}^{(j)} \right\} \cdot \left\{ \frac{6(\varepsilon^2 + 5\varepsilon + 2\varepsilon\varepsilon_\infty + \varepsilon_\infty)}{(2\varepsilon + 1)(\varepsilon + 2)(\varepsilon_\infty + 2)}\,(\bar{\mathsf{m}}^{(1)} + \bar{\mathsf{m}}^{(j)}) - (\bar{\boldsymbol{\mu}}^{(1)} + \bar{\boldsymbol{\mu}}^{(j)}) \right\} \right\rangle \qquad (27)$$

[13] Buckingham, *Proc. Roy. Soc.*, 1956, *A*, **238**, 235.

where $\overline{\overline{\mathsf{m}}}^{(1i)}$ and $\overline{\overline{\boldsymbol{\mu}}}^{(1i)}$ are the mean total and " permanent " moments of a small macroscopic sphere surrounding the fixed molecules 1 and i when these are in short range interaction with each other; $\overline{\mathsf{m}}^{(j)}$ and $\overline{\boldsymbol{\mu}}^{(j)}$ refer to the average moments of the small sphere when molecule j only is fixed. Since [13]

$$\frac{3(\varepsilon-\varepsilon_\infty)}{(\varepsilon+2)(\varepsilon_\infty+2)}=\frac{4\pi}{9kTV}\langle M^2\rangle=\frac{4\pi N}{9kTV}\left\{\frac{6(\varepsilon^2+5\varepsilon+2\varepsilon\varepsilon_\infty+\varepsilon_\infty)}{(2\varepsilon+1)(\varepsilon+2)(\varepsilon_\infty+2)}\boldsymbol{\mu}\cdot\overline{\mathsf{m}}-\boldsymbol{\mu}\cdot\overline{\boldsymbol{\mu}}\right\} \quad (28)$$

eqn. (27) becomes

$$f=\frac{2(\varepsilon-\varepsilon_\infty)}{(\varepsilon+2)(\varepsilon_\infty+2)}\frac{9kTV}{4\pi N}\left\{1+\sum_j{}''\langle\cos\theta^{(1j)}\rangle\right\}$$
$$+\frac{1}{\mu^2}\sum_{i\neq 1}{}'\left\langle\left\{\boldsymbol{\mu}^{(1)}\cdot\boldsymbol{\mu}^{(i)}\boldsymbol{\mu}^{(1)}-\tfrac{1}{3}\mu^2\boldsymbol{\mu}^{(i)}\right\}\cdot\left\{\frac{6(\varepsilon^2+5\varepsilon+2\varepsilon\varepsilon_\infty+\varepsilon_\infty)}{(2\varepsilon+1)(\varepsilon+2)(\varepsilon_\infty+2)}\overline{\overline{\mathsf{m}}}^{(1i)}-\overline{\overline{\boldsymbol{\mu}}}^{(1i)}\right\}\right\rangle \quad (29)$$

Now

$$\sum_j{}''\langle\cos\theta^{(1j)}\rangle=\frac{1}{\mu^2}\langle\boldsymbol{\mu}^{(1)}\cdot(\mathsf{M}-\mathsf{M}'-\overline{\boldsymbol{\mu}}^{(1)})\rangle$$
$$=-\frac{6(\varepsilon-1)(\varepsilon-\varepsilon_\infty)}{(2\varepsilon+1)(\varepsilon+2)(\varepsilon_\infty+2)}\frac{\boldsymbol{\mu}\cdot\overline{\mathsf{m}}}{\mu^2} \quad . \quad . \quad . \quad (30)$$

so that the general microscopic expression for f is

$$f=\frac{(\varepsilon-\varepsilon_\infty)}{(\varepsilon+2)(\varepsilon_\infty+2)}\frac{9kTV}{2\pi N}\left\{1-\frac{6(\varepsilon-1)(\varepsilon-\varepsilon_\infty)}{(2\varepsilon+1)(\varepsilon+2)(\varepsilon_\infty+2)}\frac{\boldsymbol{\mu}\cdot\overline{\mathsf{m}}}{\mu^2}\right\}$$
$$+\frac{1}{\mu^2}\sum_{i\neq 1}{}'\left\langle\left\{\boldsymbol{\mu}^{(1)}\cdot\boldsymbol{\mu}^{(i)}\boldsymbol{\mu}^{(1)}-\tfrac{1}{3}\mu^2\boldsymbol{\mu}^{(i)}\right\}\cdot\left\{\frac{6(\varepsilon^2+5\varepsilon+2\varepsilon\varepsilon_\infty+\varepsilon_\infty)}{(2\varepsilon+1)(\varepsilon+2)(\varepsilon_\infty+2)}\overline{\overline{\mathsf{m}}}^{(1i)}-\overline{\overline{\boldsymbol{\mu}}}^{(1i)}\right\}\right\rangle \quad (31)$$

For polar substances, eqn. (17) can be expressed approximately in the form

$${}_mK=\frac{2\pi N}{405}\left[2\gamma_{\alpha\alpha\beta\beta}+\frac{4}{kT}\frac{9\varepsilon}{(2\varepsilon+1)(\varepsilon+2)}\beta_{\alpha\alpha\beta}\overline{\mathsf{m}}_\beta+\right.$$
$$\left.\frac{3}{kT}\left(\sum_{s=1}^{3}\alpha_s\alpha_s^{(0)}-3\alpha\alpha^{(0)}\right)+\frac{9}{2(kT)^2}(\alpha_1-\alpha)f\right] \quad . \quad . \quad (32)$$

where f is related to microscopic quantities by eqn. (31).

Application to Polar Substances.—We shall use Onsager's model [14] of a polar liquid to evaluate eqn. (32). As this model represents the immediate surroundings of a molecule by a continuum of dielectric constant ε it excludes all short range orientational forces. We may therefore neglect the second term of f in eqn. (31). Also, for this model

$$\mathsf{m}=\frac{(2\varepsilon+1)(\varepsilon_\infty+2)}{3(2\varepsilon+\varepsilon_\infty)}\boldsymbol{\mu} \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (33)$$

so that eqn. (31) becomes

$$f=\frac{27kTV}{2\pi N}\frac{\varepsilon(\varepsilon-\varepsilon_\infty)}{(\varepsilon+2)^2(2\varepsilon+\varepsilon_\infty)} \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (34)$$

The Kerr constant may now be written as

$${}_mK=\frac{2\pi N}{405}\left[2\gamma_{\alpha\alpha\beta\beta}+\frac{12}{kT}\frac{\varepsilon(\varepsilon_\infty+2)}{(\varepsilon+2)(2\varepsilon+\varepsilon_\infty)}\beta_{\alpha\alpha\beta}\bar{\mu}_\beta+\right.$$
$$\left.\frac{3}{kT}\left(\sum_{s=1}^{3}\alpha_s\alpha_s^{(0)}-3\alpha\alpha^{(0)}\right)+\frac{9}{2(kT)^2}(\alpha_1-\alpha)f\right] \quad . \quad . \quad (35)$$

[14] Onsager, *J. Amer. Chem. Soc.*, 1936, **58**, 1486.

If we ignore the β and γ terms, and in the absence of reliable information about their magnitudes it is difficult to do otherwise, eqn. (35) reduces to

$$ {}_{\mathrm{m}}K = \frac{2\pi N}{135kT}\left[\sum_{s=1}^{3}\alpha_s\alpha_s^{(0)} - 3\alpha\alpha^{(0)} + \frac{3}{2kT}(\alpha_1 - \alpha)f\right] \quad . \quad . \quad . \quad (36) $$

For evaluating ${}_{\mathrm{m}}K$ at different temperatures through eqn. (36), we used eqn. (34), and in addition supposed that

$$ \sum_{s=1}^{3}\alpha_s\alpha_s^{(0)} - 3\alpha\alpha^{(0)} = \tfrac{3}{2}(\alpha_1 - \alpha)(\alpha_1^{(0)} - \alpha^{(0)}) \quad . \quad . \quad . \quad . \quad . \quad . \quad (37) $$

which is precise for axially symmetric molecules. It is in principle possible to determine $(\alpha_1 - \alpha)$ and $\sum_{s=1}^{3}\alpha_s\alpha_s^{(0)} - 3\alpha\alpha^{(0)}$ in the general case through the constant for the gas ${}_{\mathrm{m}}K_{\mathrm{g}}$ and the dilute-solution value ${}_{\infty}({}_{\mathrm{m}}K_2)$, but this procedure is unnecessary, as the use of eqn. (37), together with the assumption that $\alpha_s^{(0)} = \alpha_s$, does not significantly affect the results; this is because both of these simplifications influence only the term of $0(\alpha^2)$ in eqn. (36).

We used the solution results to calculate $(\alpha_1 - \alpha)$ from

$$ {}_{\mathrm{m}}K = \frac{\pi N}{45kT}(\alpha_1 - \alpha)\left[(\alpha_1 - \alpha) + \frac{f}{kT}\right] \quad . \quad . \quad . \quad . \quad . \quad . \quad (38) $$

and [4]

$$ f_{\mathrm{soln.}} = (2/3)\ {}_{\infty}\mu^2_{\mathrm{soln.}} \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (39) $$

(see Table 2). ${}_{\infty}\mu_{\mathrm{soln.}}$ is the apparent dipole moment of a polar solute molecule in a non-polar solvent at infinite dilution. We then compared the values of ${}_{\mathrm{m}}K_{\mathrm{g}}$, calculated from

TABLE 2. *Calculations of* $(\alpha_1 - \alpha)$ *from* ${}_{\infty}({}_{\mathrm{m}}K_2)$ *in* CCl_4 *at* 20°.

Substance	μ (D)	$\frac{{}_{\infty}\mu^2_{\mathrm{soln.}}}{\mu^2}$ [12]	$10^{12}\ {}_{\infty}({}_{\mathrm{m}}K_2)$ (e.s.u.) [12]	$10^{24}(\alpha_1 - \alpha)$ (cm.^{3})
$CHCl_3$	1·02	1·1	−28·5	$-1{\cdot}58_9$
$(CH_3)_2CO$	2·89	0·90	101	$0{\cdot}78_0$
$C_6H_5{\cdot}NO_2$	4·24	0·87	1073	$3{\cdot}94_9$
C_6H_5Cl	1·73	0·83	145	$3{\cdot}16_6$

TABLE 3. *Calculations of* ${}_{\mathrm{m}}K_{\mathrm{g}}$.

Substance	Temp.	$10^{12}\ {}_{\mathrm{m}}K_{\mathrm{g}}$ (e.s.u.) (Calc.)	$10^{12}\ {}_{\mathrm{m}}K_{\mathrm{g}}$ (e.s.u.) [15] (Obs.)
$CHCl_3$	89·5°	−16·4	−16·96
$(CH_3)_2CO$	83·1	76·0	69·47
$C_6H_5{\cdot}NO_2$	235·5	413	451·1
C_6H_5Cl	153·7	83·6	96·45

TABLE 4. *Calculations of* ${}_{\mathrm{m}}K_{\mathrm{liq.}}$ *for polar liquids.*

Substance	Temp.	$10^{12}\ {}_{\mathrm{m}}K_{\mathrm{liq.}}$ (e.s.u.) (Calc.)	$10^{12}\ {}_{\mathrm{m}}K_{\mathrm{liq.}}$ (e.s.u.) [12] (Obs.)
$CHCl_3$	25°	−16·9	−14·0
$(CH_3)_2CO$	20	8·31	8·33
$C_6H_5{\cdot}NO_2$	23	50·3	70·9
C_6H_5Cl	23·5	61·2	57·7

eqn. (38) with $f_{\mathrm{gas}} = 2\mu^2/3$, and ${}_{\mathrm{m}}K_{\mathrm{liq.}}$, calculated from eqns. (38) and (34), with the experimental results (see Tables 3 and 4).

The observed values of ${}_{\mathrm{m}}K_{\mathrm{g}}$ are those of Stuart and Volkmann;[15] the agreement shown in Table 3 illustrates the consistency of the gas and the solution data, and justifies our use of the simplifications discussed in the previous paragraph.

The agreement in Table 4 between the calculated and observed values of ${}_{\mathrm{m}}K$ for polar liquids is satisfactory, for the unknown contributions of the β and γ terms were neglected and some of the approximations inherent in the Onsager model were used.

For highly polar anisotropic molecules, ${}_{\mathrm{m}}K_{\mathrm{g}}$ is dominated by the term proportional to T^{-2}. Hence for liquids consisting of molecules of this type, eqn. (38) yields

$$\frac{{}_{\mathrm{m}}K_{\mathrm{liq.}}}{{}_{\mathrm{m}}K_{\mathrm{g}}} = \frac{3kT}{2\mu^2}(\alpha_1 - \alpha) + \frac{81kTV}{4\pi N\mu^2}\frac{\varepsilon(\varepsilon - \varepsilon_\infty)}{(\varepsilon + 2)^2(2\varepsilon + \varepsilon_\infty)} \quad . \quad . \quad . \quad (40)$$

Eqn. (40) can be put into a form similar to an expression deduced by Klages,[2] by means of the assumption that μ is related to ε by the Onsager relation

$$\frac{4\pi N\mu^2}{9kTV} = \frac{(\varepsilon - \varepsilon_\infty)(2\varepsilon + \varepsilon_\infty)}{\varepsilon(\varepsilon_\infty + 2)^2} \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (41)$$

The second term in eqn. (40) then becomes $\left[\frac{3\varepsilon(\varepsilon_\infty + 2)}{(\varepsilon + 2)(2\varepsilon + \varepsilon_\infty)}\right]^2$ which is Klages's result.

Application to Water.—In applying the theory for polar substances to water, we shall employ the Pople model[16] of the structure of water to evaluate the short-range interaction terms in eqn. (31). In this model a water molecule influences, through hydrogen bonding, its neighbours in the first three shells only, and these contain approximately 4, 11, and 22 molecules. Thus our macroscopic sphere containing all short-range effects consists of a central molecule and its first three shells of neighbours.

$\boldsymbol{\mu} \cdot \bar{\mathbf{m}}$ in eqn. (31) may be expressed through eqn. (28) in terms of $\boldsymbol{\mu} \cdot \bar{\boldsymbol{\mu}}$, which was evaluated by Pople.[16] We shall write

$$\frac{\boldsymbol{\mu} \cdot \bar{\boldsymbol{\mu}}}{\mu^2} = g = \sum_i{}' \left\langle \cos\theta^{(1i)} \right\rangle . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (42)$$

To evaluate the second term in eqn. (31), we use the Onsager result (33). This is believed to be a good approximation for water.[13] Thus

$$\sum_{i\neq 1}{}' \left\langle \left\{ \boldsymbol{\mu}^{(1)} \cdot \boldsymbol{\mu}^{(i)}\boldsymbol{\mu}^{(1)} - \tfrac{1}{3}\mu^2\boldsymbol{\mu}^{(i)} \right\} \cdot \left\{ \frac{6(\varepsilon^2 + 5\varepsilon + 2\varepsilon\varepsilon_\infty + \varepsilon_\infty)}{(2\varepsilon + 1)(\varepsilon + 2)(\varepsilon_\infty + 2)} \bar{\bar{\mathbf{m}}}^{(1i)} - \bar{\bar{\boldsymbol{\mu}}}^{(1i)} \right\} \right\rangle$$

$$= \frac{3\varepsilon(\varepsilon_\infty + 2)}{(\varepsilon + 2)(2\varepsilon + \varepsilon_\infty)} \sum_{i\neq 1}{}' \left\langle \boldsymbol{\mu}^{(1)} \cdot \boldsymbol{\mu}^{(i)}\boldsymbol{\mu}^{(1)} \cdot \bar{\bar{\boldsymbol{\mu}}}^{(1i)} - \tfrac{1}{3}\mu^2\boldsymbol{\mu}^{(i)} \cdot \bar{\bar{\boldsymbol{\mu}}}^{(1i)} \right\rangle . \quad . \quad (43)$$

and

$$\sum_{i\neq 1}{}' \left\langle \boldsymbol{\mu}^{(1)} \cdot \boldsymbol{\mu}^{(i)}\boldsymbol{\mu}^{(1)} \cdot \bar{\bar{\boldsymbol{\mu}}}^{(1i)} - \tfrac{1}{3}\mu^2\boldsymbol{\mu}^{(i)} \cdot \bar{\bar{\boldsymbol{\mu}}}^{(1i)} \right\rangle = \mu^4 \sum_{i\neq 1}{}' \left[\tfrac{2}{3}\left\langle \cos\theta^{(1i)} \right\rangle + \left\langle \cos^2\theta^{(1i)} - \tfrac{1}{3} \right\rangle \right.$$

$$\left. + \sum_{j\neq 1,i}{}' \left\langle \cos\theta^{(1i)} \cos\theta^{(1j)} - \tfrac{1}{3}\cos\theta^{(ij)} \right\rangle \right] \quad . \quad . \quad . \quad (44)$$

Now

$$\sum_{i\neq 1}{}' \left[\tfrac{2}{3}\left\langle \cos\theta^{(1i)} \right\rangle + \left\langle \cos^2\theta^{(1i)} - \tfrac{1}{3} \right\rangle \right] =$$

$$\tfrac{2}{3}\sum_{K=1}^{3} N^{(K)} \left\langle \cos\theta_K^{(12)} \right\rangle + \sum_{K=1}^{3} N^{(K)} \left\langle \cos^2\theta_K^{(12)} - \tfrac{1}{3} \right\rangle \quad . \quad . \quad (45)$$

where $N^{(K)}$ is the number of molecules in the K-th shell, and $\theta_K^{(12)}$ is the angle between the permanent dipoles of molecule 1 and molecule 2 in the K-th shell around 1.

[15] Stuart and Volkmann, *Ann. Physik*, 1933, **18**, 121.
[16] Pople, *Proc. Roy. Soc.*, 1951, *A*, **205**, 163.

The averages in eqn. (45) have been evaluated for Pople's model and are

$$\left\langle \cos\theta_K^{(12)} \right\rangle = 3^{1-K} \cos^{2K}\frac{\beta}{2}\left[1-\frac{kT}{G}\right]^{2K} \quad . \quad . \quad . \quad . \quad (46)$$

$$\left\langle \cos^2\theta_1^{(12)} \right\rangle = \left[\tfrac{3}{2}\cos^4\frac{\beta}{2} - \cos^2\frac{\beta}{2}\right]\left[1-\frac{3kT}{G}\left(1-\frac{kT}{G}\right)\right]^2 + \tfrac{1}{2}\left[1-\frac{2kT}{G}\left(1-\frac{kT}{G}\right)+3\left\{\frac{kT}{G}\left(1-\frac{kT}{G}\right)\right\}^2\right] \quad . \quad . \quad . \quad (47)$$

$$\left\langle \cos^2\theta_2^{(12)} \right\rangle = \tfrac{1}{2} - \left\langle \cos^2\theta_1^{(12)} \right\rangle + \tfrac{3}{2}\left(\left\langle \cos^2\theta_1^{(12)} \right\rangle\right)^2 \quad . \quad . \quad . \quad . \quad (48)$$

$$\left\langle \cos^2\theta_3^{(12)} \right\rangle = \tfrac{9}{4}\left(\left\langle \cos^2\theta_1^{(12)} \right\rangle\right)^3 - \tfrac{9}{4}\left(\left\langle \cos^2\theta_1^{(12)} \right\rangle\right)^2 + \tfrac{3}{4}\left\langle \cos^2\theta_1^{(12)} \right\rangle + \tfrac{1}{4} \quad (49)$$

where β is the observed value of the H–O–H angle, 105° (β is also the angle between the lone-pair orbitals), and G is a temperature-dependent constant, chosen by Pople to give agreement between the theoretical and experimental radial distribution functions.

For the approximate evaluation of $\langle \cos\theta^{(1i)}\cos\theta^{(1j)} - \frac{1}{3}\cos\theta^{(ij)}\rangle$ in eqn. (44) we shall consider only first neighbours of molecules 1 and i. When molecule j belongs to the same shell as i (relative to molecule 1), then the last term of eqn. (44) vanishes. Thus it can be shown that for this model

$$\sum_{i\neq 1}'\sum_{j\neq 1,i}'\left\langle \cos\theta^{(1i)}\cos\theta^{(1j)} - \tfrac{1}{3}\cos\theta^{(ij)} \right\rangle = \sum_{i\neq 1}'\sum_{j\neq 1,i}'\left\langle \cos\theta^{(ij)}\right\rangle\left\langle \cos^2\theta^{(1i)} - \tfrac{1}{3}\right\rangle \quad (50)$$

where i and j are summed over molecules in the first and second shells respectively.

The contribution at 0° c to eqn. (44) of each of its terms is shown as follows :

	Shell 1	Shell 2	Shell 3
$N^{(K)}\left\langle \cos\theta_K^{(12)} \right\rangle$	1·201	0·330	0·067
$N^{(K)}\left\langle \cos^2\theta_K^{(12)} - \frac{1}{3} \right\rangle$	$4{\cdot}4 \times 10^{-3}$	2×10^{-5}	3×10^{-7}
$\sum_{i\neq 1}'\sum_{j\neq 1,i}'\left\langle \cos\theta^{(1i)}\cos\theta^{(1j)} - \frac{1}{3}\cos\theta^{(ij)} \right\rangle$	5×10^{-3}	—	

(We have used $G/kT = 10$, as found by Pople for 0°.)

We note that $\sum_{i\neq 1}'\left\langle \cos^2\theta^{(1i)} - \frac{1}{3}\right\rangle$ and $\sum_{i\neq 1}'\sum_{j\neq 1,i}'\left\langle \cos\theta^{(1i)}\cos\theta^{(1j)} - \frac{1}{3}\cos\theta^{(ij)}\right\rangle$ are together less than 1% of $\frac{2}{3}\sum_{i\neq 1}'\left\langle \cos\theta^{(1i)}\right\rangle$ for water at 0°, and may therefore reasonably be neglected. (Some further justification for our neglect of $\iint(\cos^2\theta_{si} - \frac{1}{3})n_2(\mathbf{r},\omega)\mathrm{d}\mathbf{r}\,\mathrm{d}\omega$ in the derivation of eqn. (20) is provided by these calculations for water.)

Thus eqn. (43) becomes

$$\frac{3\varepsilon(\varepsilon_\infty+2)}{(\varepsilon+2)(2\varepsilon+\varepsilon_\infty)}\sum_{i\neq 1}'\left\langle \boldsymbol{\mu}^{(1)}\cdot\boldsymbol{\mu}^{(i)}\boldsymbol{\mu}^{(1)}\cdot\overline{\overline{\boldsymbol{\mu}}}^{(1i)} - \tfrac{1}{3}\mu^2\boldsymbol{\mu}^{(i)}\cdot\overline{\overline{\boldsymbol{\mu}}}^{(1i)}\right\rangle = \frac{2\varepsilon(\varepsilon_\infty+2)}{(\varepsilon+2)(2\varepsilon+\varepsilon_\infty)}\mu^4(g-1) \quad . \quad . \quad (51)$$

Hence for water, eqn. (31) is given approximately by

$$f = \frac{9kTV}{2\pi N}\frac{(\varepsilon-\varepsilon_\infty)}{(\varepsilon+2)(\varepsilon_\infty+2)}\left[1-\frac{6(\varepsilon-1)(\varepsilon-\varepsilon_\infty)}{(2\varepsilon+1)(\varepsilon+2)(\varepsilon_\infty+2)}\frac{\boldsymbol{\mu}\cdot\overline{\mathbf{m}}}{\mu^2}\right] + \frac{2\varepsilon(\varepsilon_\infty+2)}{(\varepsilon+2)(2\varepsilon+\varepsilon_\infty)}\mu^2(g-1) \quad . \quad . \quad (52)$$

In the absence of data on hyperpolarizability, we shall approximate the expression for the Kerr constant to

$$ {}_{m}K = \frac{\pi N}{45(kT)^2}(\alpha_1 - \alpha)f \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (53) $$

We have omitted terms in higher powers of the polarizability, but this should be reasonable for water with its small value for α. From eqn. (53) we can predict the value of ${}_{m}K$ for

TABLE 5. *Temperature dependence of* ${}_{m}K_{liq.}$ *for water.*

Temp.	V_m (cm.^{3})	ε	ε_∞	g	$10^{37}<M_1^2 - M^2/3>$ (e.s.u.)	${}_{m}K_T/{}_{m}K_0$
0°	18·02	88·2	$1{\cdot}79_7$	2·60	$-3{\cdot}66_9$	1·000
25	18·07	78·5	$1{\cdot}79_5$	2·55	$-3{\cdot}71_9$	0·851
62	18·34	66·4	$1{\cdot}78_0$	2·49	$-3{\cdot}82_2$	0·692
83	18·58	60·4	$1{\cdot}76_7$	2·46	$-3{\cdot}87_4$	0·621

water at a given temperature in terms of its value ${}_{m}K_0$ at 0°; the results are shown in Table 5. We have taken μ to be 1·84 D. The ε values are those of Wyman and Ingalls,[17] and the g's are Pople's. Unfortunately there are at present no data to test our predictions.

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[17] Wyman and Ingalls, *J. Amer. Chem. Soc.*, 1938, **60**, 1182.

450. *The Preparation of Chloro-bridged Complexes of Palladium*(II) *containing Uncharged Monodentate Ligands having Nitrogen, Phosphorus, Arsenic, Antimony, Sulphur, Selenium, and Tellurium as Donor Atoms.*

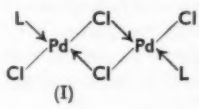
By J. CHATT and L. M. VENANZI.

A series of chloro-bridged complex compounds of the type $[L_2Pd_2Cl_4]$ (I) has been prepared. These contain amines, tertiary organic phosphines, arsines, or stibines, or dialkyl sulphides, selenides, or tellurides as the ligands L.

The amine complexes are somewhat anomalous, but the remainder form two well-graded series, according to the positions of the donor atoms of L in the Periodic Table. Generally the bridged complexes are less stable than their platinous analogues, but the selenide bridged complexes ($L = R_2Se$) are more stable.

A SERIES of chloro-bridged complexes of the type $[L_2Pd_2Cl_4]$ (I) was necessary to our studies [1] of the inductive and mesomeric effects of a series of uncharged ligands L, and here we describe their preparation and properties. In formula (I), L is an uncharged ligand of the type amine, tertiary organic phosphine, arsine, or stibine, dialkyl sulphide, selenide, or telluride.

Many binuclear complexes of palladium(II), containing tertiary phosphines and arsines as the ligand L, have been described [2] and their *trans*-symmetrical structures (I) are well established.[3] The most general method of preparation, developed by Mann and his co-workers, consists of boiling under reflux an aqueous-alcoholic solution of equimolecular proportions of the simple complex L_2PdCl_2 and ammonium chloropalladite. This reaction is complete in 0·5—1·5 hr. and can be written :



(I)

$$ L_2PdCl_2 + (NH_4)_2PdCl_4 \longrightarrow L_2Pd_2Cl_4 + 2NH_4Cl \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (1) $$

[1] Chatt, Duncanson, and Venanzi, *J.*, 1955, 4461.
[2] Mann, *Ann. Reports*, 1938, **35**, 148; Gmelin. "Handbuch der anorganischen Chemie. Palladium." System no. 65, pp. 422—432, Verlag Chemie, Berlin, 1942.
[3] Mann and Wells, *J.*, 1938, 702; Wells, *Proc. Roy. Soc.*, 1938, *A*, **167**, 169.

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It is readily applicable to the preparation of the bridged complexes of tertiary phosphines and arsines, but not to the less stable bridged complexes, such as we have now prepared (see Table 1). These are better prepared by a simple modification using sodium chloropalladite, instead of the ammonium salt, in ethanol or acetone at room temperature. The reaction then requires a few hours to a few days for completion, but it appears to have universal application, except to bridged complexes (I) in which L is an olefin or an amine. The reaction is carried out at a temperature consistent with the stability of the product, and may occur according to equation (2) or (3), depending on the starting materials available:

$$L_2PdCl_2 + Na_2PdCl_4 \longrightarrow L_2Pd_2Cl_4 + 2NaCl \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (2)$$

$$2L + 2Na_2PdCl_4 \longrightarrow L_2Pd_2Cl_4 + 4NaCl \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (3)$$

The ease with which the chloro-bridged complexes of palladium(II) are obtained is in marked contrast to the more difficult preparation of the analogous platinum(II) complexes where a variety of methods is used to prepare the complete series.[4] The bridged complexes prepared in this research are listed in the Table, together with their methods of preparation. A few known phosphine and arsine members of the series are included there for comparison.

Preparation of Amine Chloro-bridged Complexes (I; L = amine).—This was difficult. Only di-*n*-pentylamine and piperidine of the amines tried gave products of the correct composition; and the piperidine complex is probably a polymer, being obtained as a light brown insoluble precipitate by the reaction of equimolecular proportions of [piperidine$_2$PdCl$_2$] or of piperidine itself with sodium chloropalladite in alcohol. Its insolubility is in marked contrast to the solubility of its platinous analogue which is known to be dimeric. It therefore seems improbable that the palladium complex is a binuclear

Halogen-bridged complexes of palladium(II).

Complex	Method *	M. p.	Colour
{PiperidinePdCl$_2$}$_x$ †	A and B	178—180° (decomp.)	Brown
{NH(*n*-C$_5$H$_{11}$)$_2$}$_2$Pd$_2$Cl$_4$ †	B	178—181·5 (decomp.)	Ochre
(PEt$_3$)$_2$Pd$_2$Cl$_4$	A and B	230	Orange
(PPr$^n_3$)$_2$Pd$_2$Cl$_4$	A	189—191	Orange
(PBu$^n_2$Ph)$_2$Pd$_2$Cl$_4$ †	B	193—193·5	Reddish-orange
(PPh$_3$)$_2$Pd$_2$Cl$_4$	A and B	Decomp. *ca.* 250—270	Brownish-orange
{P(MeO)$_3$}$_2$Pd$_2$Cl$_4$ §	B	114—115	Yellowish-orange
{P(PhO)$_3$}$_2$Pd$_2$Cl$_4$ †	B	168—171	Yellowish-orange
(AsPr$^n_3$)$_2$Pd$_2$Cl$_4$	B	159—160	Dark orange
(SbEt$_3$)$_2$Pd$_2$Cl$_4$ †	B	87—88 (decomp.)	Dark red
(Et$_2$S)$_2$Pd$_2$Cl$_4$ ‡	A and B	143—144·5	Tan
(Pr$^n_2$S)$_2$Pd$_2$Cl$_4$ †	B	80—81	Tan
(Et$_2$Se)$_2$Pd$_2$Cl$_4$ †	A and B	148·5—150	Reddish-brown
(Pr$^n_2$Se)$_2$Pd$_2$Cl$_4$ †	B	86·5—87	Reddish-brown
(Et$_2$Te)$_2$Pd$_2$Cl$_4$ †	A and B	110—125 (decomp.)	Dark reddish-brown
(Pr$^n_2$Te)$_2$Pd$_2$Cl$_4$ †	B	131·5—132 (decomp.)	Dark reddish-brown
(PPr$^n_3$)$_2$Pd$_2$Br$_4$ †	B	178—179	Dark red
(PPr$^n_3$)$_2$Pd$_2$I$_4$ †	B	202—203	Purple-black

* A, prepared by reaction 2; B, prepared by reaction 3. † New compounds. ‡ Prepared by Ardell, "Palladiumsalters föreningar med alkylsulfider," Akad. Afhandl. Lund, 1896, p. 9 and formulated as the "double salt" [Pd(Et$_2$S)$_2$Cl$_2$]PdCl$_2$. § Prepared by Fink (*Compt. rend.*, 1892, **115**, 176) but not characterised.

complex of the usual type. Nevertheless, when it is treated with triphenylphosphine it gives some *trans*-[Ph$_3$P,piperidinePdCl$_2$] identical with the compound prepared from [(Ph$_3$P)$_2$Pd$_2$Cl$_4$] and piperidine. The di-*n*-pentylamine complex, similarly prepared, was soluble in some organic solvents and its molecular weight and composition indicated the formula [{NH(C$_5$H$_{11}$)$_2$}$_2$Pd$_2$Cl$_4$] in solution.

Attempts to obtain [(4-*n*-pentylpyridine)$_2$Pd$_2$Cl$_4$] by methods A and B led to the recovery of the simple complex, [(4-*n*-pentylpyridine)$_2$PdCl$_2$]. The following methods also failed: (*a*) boiling an acetone solution of pentylpyridine (1 mol.) and sodium chloropalladite (1 mol.) under reflux for 3 hr.; (*b*) fusion of [(4-*n*-pentylpyridine)$_2$PdCl$_2$] with

[4] Chatt and Venanzi, *J.*, 1955, 2787.

powdered palladous chloride; (*c*) heating the simple pentylpyridine complex above its melting point under a high vacuum for 2 hr.[5] In all cases the unchanged mononuclear complex was recovered. This failure to prepare $[(4\text{-}n\text{-pentylpyridine})_2Pd_2Cl_4]$ is somewhat puzzling. In the platinous series, amine compounds of this type are prepared by the spontaneous decomposition of the mixed olefin complex, *trans*-[olefin,am$PtCl_2$] (where am = amine), in a solvent where the bridged complex $[am_2Pt_2Cl_4]$ is insoluble.[4] Attempts to use this route in the palladous series were frustrated by the impossibility of obtaining complexes of the type [olefin,am$PdCl_2$]. Two methods were tried and many attempts were made to apply them. In the first a solution of $[(cyclo\text{hexene})_2Pd_2Cl_4]$ [6] in methylene chloride was treated at −70° with a cold solution of *p*-toluidine in methylene chloride, but the solution blackened immediately after the first addition. Attempts to prepare $[C_2H_4,amPdCl_2]$, *via* $K[C_2H_4PdCl_3]$ in analogous manner to the platinum complex,[7] in water and in the presence of hydrochloric and of perchloric acid respectively led to instantaneous evolution of ethylene.

Properties of the Chloro-bridged Complexes of Palladium(II).—These complexes are beautifully crystalline and usually deeper in colour and more soluble in organic solvents than their platinous analogues.[4] They show well-graded properties according to the Groups of donor atoms P, As, and Sb, and S, Se, and Te contained in them. The stabilities decrease and the colours become more intense on ascending each Group. The stabilities of the complexes lie roughly in the order of donor atoms P > As ~ S > Se > Te > Sb. The crystalline triethylstibine complex is very unstable in moist air, becoming semiliquid and liberating the stibine. Stored in a desiccator it decomposes in 2—3 days. It is also to be noted that the melting points of the arsine complexes are lower than those of their phosphine analogues, yet those of the selenide complexes are higher than those of their sulphide analogues. Generally the chloro-bridged complexes of palladium(II) are rather less stable than those of platinum, with the notable exception of the dialkyl selenide complexes which are considerably more stable.

In the platinous series of chloro-bridged complexes of the type $[L_2Pt_2Cl_4]$ the selenide complexes (L = Et_2Se) are very unstable, so that the stabilities of the complexes are in order of ligands L, $R_2S \gg R_2Se < R_2Te$.[1] In the palladous series the stabilities of the selenide complexes are truly intermediate, so that the sequence is $R_2S > R_2Se > R_2Te$. This difference in the sequence of stabilities may depend on the relative sizes of the orbitals used in forming the co-ordinate σ-bonds. It may be that those of selenium are comparable with those of palladium and those of tellurium with platinum and the strengths of the Se–Pd and Te–Pt bonds may be enhanced by this. This could account for the irregular order of stabilities observed in the platinous series and its absence in the analogous palladous series. It is remarkable that the irregularity in the platinous series also extends to the colours of the complexes, *e.g.*, $[(Et_2S)_2Pt_2Cl_4]$ is bright yellow whereas the selenium and tellurium analogues are both a dull brownish-orange.[4] In the palladous series the corresponding compounds grade uniformly from a light tan colour (S) through reddish-brown (Se) to a dark reddish-brown (Te) (see Table).

Experimental

Microanalyses are by Messrs. W. Brown and A. G. Olney of these laboratories.

The known mononuclear complexes $[L_2PdCl_2]$ used in the preparations described below, except those whose preparations are given, were prepared by adding two equivalents of the ligand L to an alcoholic solution of sodium chloropalladite tetrahydrate.

Bis(diethyl telluride)dichloropalladium, $[(Et_2Te)_2PdCl_2]$.—Ammonium chloropalladite (3·2 g.) in water (20 c.c.) was treated with diethyl telluride (3·8 g.) in a nitrogen atmosphere. After a few minutes' shaking a dark orange precipitate was formed. This was filtered off, washed with water, ethanol, and ether, and dried. Recrystallised three times from methanol, the

[5] Cf. Mann and Purdie, *J.*, 1936, 873.
[6] Kharasch, Seyler, and Mayo, *J. Amer. Chem. Soc.*, 1938, **60**, 882.
[7] Chatt, *J.*, 1949, 3340.

product was obtained as deep reddish-orange plates, m. p. 98·5—99° (28%) (Found: C, 17·7; H, 3·7. $C_8H_{20}Cl_2PdTe_2$ requires C, 17·5; H, 3·7%).

The simple complexes of amines, $[am_2PdCl_2]$, were prepared by treating the palladite in aqueous solution with an excess of the amine until a colourless solution of the salt $[Pd\,am_4]Cl_2$ had been formed, and decomposing this salt by concentrated hydrochloric acid. The orange solid, which separated, was filtered off, dried, and recrystallised from a suitable solvent. In this way were prepared dipiperidinedichloropalladium, $[(C_5H_{11}N)_2PdCl_2]$, orange needles (from methanol), decomp. 175—189° (yield 52%) (Found: C, 34·7; H, 6·25; N, 8·4. Calc. for $C_{10}H_{22}N_2Cl_2Pd$: C, 34·5; H, 6·4; N, 8·05%), and *bis*-4-n-*pentylpyridinedichloropalladium*, $[(C_{10}H_{15}N)_2PdCl_2]$, orange leaflets (from methanol), m. p. 145° (sinters at 143·5°) (56%) (Found: C, 50·2; H, 6·4; N, 5·9. $C_{20}H_{30}N_2Cl_2Pd$ requires C, 50·45; H, 6·35; N, 5·9%). The two amine complexes are non-electrolytes in nitrobenzene solution.

Preparation of the Chloro-bridged Complexes by Method A.—Reaction between [(piperidine)$_2PdCl_2$] *and sodium chloropalladite.* Dipiperidinedichloropalladium (1 g.) in ethanol (100 c.c.) and chloroform (50 c.c.) was treated with sodium chloropalladite tetrahydrate (0·7 g.) in ethanol and left at room temperature for 3 days. A brown solid formed was filtered off and dried *in vacuo*. It decomposed at ~180° and was insoluble in all solvents tried except pyridine, from which it could not be recovered. A sample was washed in water, ethanol, and chloroform and then dried. It is probably slightly impure $[piperidinePdCl_2]_x$ (Found: C, 24·1; H, 4·6; N, 5·4. Calc. for $C_5H_{11}NCl_2Pd$: C, 22·85; H, 4·2; N, 5·3%).

Reaction of $[piperidinePdCl_2]_x$ *with triphenylphosphine.* A suspension of the above brown solid (0·5 g.) in a solution of triphenylphosphine (0·5 g.) in acetone (50 c.c.) was shaken until the brown solid had disappeared, leaving a greenish-yellow solid (not investigated) and an orange solution. The solution was evaporated to dryness at 15 mm. and the yellow residue recrystallised from light petroleum (b. p. 80—100°). The yellowish-orange product was $[PPh_3$,piperidine$PdCl_2]$, and decomposed at 160—172° alone and mixed with an authentic specimen.

Bis(triethylphosphine)dichloro-μμ-dichlorodipalladium, $[(PEt_3)_2Pd_2Cl_4]$. Hydrated sodium chloropalladite (2·1 g.) and $[(PEt_3)_2PdCl_2]$ (2·9 g.) in ethanol (180 c.c.) were boiled under reflux for 45 min., then evaporated to dryness at 15 mm. and the solid residue was washed with water, dried, and recrystallised from ethanol (yield 81%). Its tri-*n*-propyl analogue was prepared similarly in 60% yield.

Bis(triphenylphosphine)dichloro-μμ′-dichlorodipalladium, $[(PPh_3)_2Pd_2Cl_4]$. $[(PPh_3)_2PdCl_2]$ (1·5 g.) in chloroform (200 c.c.) and sodium chloropalladite hydrate (1·5 g.) in ethanol (50 c.c.) were mixed and boiled under reflux for 1 hr. The solid deposited was removed, washed with water, then with ethanol, then chloroform, dried, and precipitated with light petroleum (b. p. 40—60°) from a large volume of hot chloroform and so was obtained in reddish-orange needles which decompose gradually at >250° (yield 98%) (Found: C, 49·1; H, 3·5. Calc. for $C_{36}H_{30}Cl_4P_2Pd_2$: C, 49·2; H, 3·4%).

Bis(diethyl sulphide)dichloro-μμ′-dichlorodipalladium, $[(Et_2S)_2Pd_2Cl_4]$. $[(Et_2S)_2PdCl_2]$ (1 g.) and hydrated sodium chloropalladite (0·8 g.) were dissolved in ethanol (75 c.c.), and the solution kept for 24 hr. The mixture was then taken to dryness at 15 mm. and the residual solid washed with water, dried, and recrystallised from chloroform and light petroleum (yield 27%) (Found: C, 18·2; H, 3·8; S, 11·7. Calc. for $C_8H_{20}Cl_4S_2Pd_2$: C, 17·9; H, 3·8; S, 12·0%). Similarly prepared were *bis(diethyl selenide)dichloro-μμ′-dichlorodipalladium,* $[(Et_2Se)_2Pd_2Cl_4]$ (recrystallised from ethyl methyl ketone; yield 25%) (Found: C, 15·7; H, 3·25. $C_8H_{20}Cl_4Pd_2Se_2$ requires C, 15·3; H, 3·2%), and *bis(diethyl telluride)dichloro-μμ′-dichlorodipalladium,* $[(Et_2Te)_2Pd_2Cl_4]$ (recrystallised from methanol; yield 23%) (Found: C, 13·5; H, 2·8. $C_8H_{20}Cl_4Pd_2Te_2$ requires C, 13·2; H, 2·8%).

Preparation of the Chloro-bridged Complexes by Method B.—Reaction between piperidine and sodium chloropalladite. Piperidine (1·5 c.c.) was added to a solution of the sodium salt (5 g.) in ethanol (100 c.c.) and kept for several days. The brown solid formed was removed and dried (3·5 g.). Soluble material was extracted from it with boiling acetone, and the insoluble product washed with water and ethanol, and then dried (1·8 g.) (Found: C, 23·1; H, 4·1; N, 5·5%). It is identical with the $[piperidinePdCl_2]_x$ prepared by method A.

Bis(di-n-pentylamine)dichloro-μμ′-dichlorodipalladium, $[\{NH(C_5H_{11})_2\}_2Pd_2Cl_4]$. Di-*n*-pentylamine (0·14 c.c.) and the hydrated sodium salt (2 g.) in ethanol (50 c.c.) were left for 3 days. The red solution was filtered from a grey solid and taken to dryness at 15 mm. in the cold. The

reddish-brown residue was recrystallised three times from ethyl acetate (yield approx. 45%) (Found: C, 36·1; H, 6·7; N, 4·1%; *M*, ebullioscopic in 0·8% benzene solution, 582, 587. $C_{20}H_{46}N_2Cl_4Pd_2$ requires C, 35·9; H, 6·9; N, 4·2%; *M*, 669). It is a non-electrolyte in nitrobenzene and decomposes in boiling solvents.

Bistriethylphosphinedichloro-μμ′-dichlorodipalladium, $[(PEt_3)_2Pd_2Cl_4]$. The sodium salt (6 g.) in ethanol (100 c.c.) was treated under nitrogen with triethylphosphine (1·94 g.). The solution was filtered after 24 hr. from some whitish residue and taken to dryness at 15 mm. The residual product (68%) was treated in the same way as that prepared by method A. Its tri-*n*-propylarsine analogue was prepared similarly.

*Bis(di-*n*-butylphenylphosphine)dichloro-μμ′-dichlorodipalladium*, $[(PBu^n_2Ph)_2Pd_2Cl_4]$. Di-*n*-butylphenylphosphine (5·6 g.) was added, under nitrogen, to a solution of the sodium salt (9·3 g.) in acetone (150 c.c.), and the mixture set aside for 3 days, filtered, and taken to dryness at 15 mm. The residual *product* was recrystallised three times from propan-1-ol (yield 30%) (Found: C, 42·0; H, 5·8. $C_{28}H_{46}Cl_4P_2Pd_2$ requires C, 42·1; H, 5·8%).

Bis(triphenylphosphine)dichloro-μμ′-dichlorodipalladium, $[(PPh_3)_2Pd_2Cl_4]$. The sodium salt (4 g.) in ethanol (50 c.c.) and triphenylphosphine (3 g.) in chloroform (200 c.c.) were mixed and boiled under reflux for 2 hr. The resulting yellow solid quickly redissolved, and a reddish solid was precipitated. This was identical with the product obtained by method A, and was purified in the same way (yield 73%).

Bis(trimethyl phosphite)dichloro-μμ′-dichlorodipalladium, $[\{P(OMe)_3\}_2Pd_2Cl_4]$. This was prepared in acetone solution analogously to the triethylphosphine compound (no nitrogen atmosphere necessary) and recrystallised from toluene by precipitation with light petroleum (b. p. 60—80°) in 30% yield (Found: C, 12·2; H, 3·1%; *M*, ebullioscopic in 0·6% benzene solution, 571. Calc. for $C_6H_{18}O_6Cl_4P_2Pd_2$: C, 11·95; H, 3·0%; *M*, 603). It is a non-electrolyte in nitrobenzene.

Bis(triphenyl phosphite)dichloro-μμ′-dichlorodipalladium, $[\{P(OPh)_3\}_2Pd_2Cl_4]$, was prepared analogously to the trimethyl phosphite complex. It was recrystallised from benzene (yield 42%) (Found: C, 44·2; H, 3·2%; *M*, ebullioscopic in 0·4% benzene solution, 771. $C_{36}H_{30}O_6Cl_4P_2Pd_2$ requires C, 44·3; H, 3·1%; *M*, 986). It is a non-electrolyte in nitrobenzene.

Bis(triethylstibine)dichloro-μμ′-dichlorodipalladium, $[(SbEt_3)_2Pd_2Cl_4]$. Triethylstibine (1·1 g.) in acetone (20 c.c.) was gradually added to a stirred solution of the sodium salt (1·6 g.) in acetone (30 c.c.) at −70° under nitrogen. The mixture was then allowed to warm to room temperature and a solid began to separate. Evaporation at 15 mm. in the cold under nitrogen yielded a reddish residue. It was dissolved in warm ethyl methyl ketone, the solution cooled, and the product reprecipitated as a dark-red powder in very poor yield by addition of light petroleum (b. p. 60—80°) (Found: C, 17·7; H, 3·6. Calc. for $C_{12}H_{30}Cl_4Pd_2Sb_2$: C, 18·6; H, 3·9%. The analyst reported that the substance gained weight during weighing).

Bis(diethyl sulphide)dichloro-μμ′-dichlorodipalladium, $[(Et_2S)_2Pd_2Cl_4]$. Diethyl sulphide (1·6 g.) was added to a solution of the sodium tetrachloropalladite (5·2 g.) in ethanol (100 c.c.) and the mixture was kept for 3 days. The solid product was removed, washed with water, and then ethanol, and dried. A further small quantity was obtained from the mother-liquor. It was recrystallised from chloroform by precipitation with light petroleum (b. p. 60—80°) (yield 38%) (Found: C, 18·05; H, 3·8%). It was identical with the product obtained by method A.

Similarly prepared were: *bis(di-*n*-propyl sulphide)dichloro-μμ′-dichlorodipalladium*, $[(Pr^n_2S)_2Pd_2Cl_4]$ (recrystallised from carbon tetrachloride; yield 26%) (Found: C, 24·5; H, 4·7%; *M*, ebullioscopic in 1·4% chloroform solution, 604. $C_{12}H_{28}Cl_4S_2Pd_2$ requires C, 24·4; H, 4·8%; *M*, 592); bis(diethyl selenide)dichloro-μμ′-dichlorodipalladium, $[(Et_2Se)_2Pd_2Cl_4]$ (recrystallised from ethyl methyl ketone; yield 28%) identical with the product obtained by method A (Found: C, 15·8; H, 3·3%); bis(diethyl telluride)dichloro-μμ′-dichlorodipalladium, $[(Et_2Te)_2Pd_2Cl_4]$ (recrystallised from methanol; yield 70%), identical with the product obtained by method A (Found: C, 13·3; H, 2·9%); *bis(di-*n*-propyl telluride)dichloro-μμ′-dichlorodipalladium*, $[(Pr^n_2Te)_2Pd_2Cl_4]$ (recrystallised from methanol; yield 30%) (Found: C, 18·3; H, 3·55. $C_{12}H_{28}Cl_4Pd_2Te_2$ requires C, 18·4; H, 3·6%), and *bis(di-*n*-propyl selenide)dichloro-μμ′-dichlorodipalladium*, $[(Pr^n_2Se)_2Pd_2Cl_4]$. In the last case no precipitate of the binuclear complex was formed during the reaction. After evaporation of the solvent at 15 mm. the brown residual product was recrystallised from carbon tetrachloride (yield 45%) (Found: C, 21·0; H, 4·1%; *M*, ebullioscopic in 1·0% chloroform solution, 660. $C_{12}H_{28}Cl_4Pd_2Se_2$ requires C, 21·0; H, 4·1%; *M*, 686).

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*Bis(tri-*n*-propylphosphine)dibromo-μμ'-dibromodipalladium*, $[(PPr^n_3)_2Pd_2Br_4]$.—Lithium bromide (12 g.) and sodium tetrachloropalladite hydrate (10 g.) were dissolved in ethanol, and tri-*n*-propylphosphine (4·4 g.) added to this solution under nitrogen. The mixture was then boiled under reflux for 4 hr. The resultant solution was taken to dryness at 15 mm. and the residual *product* recrystallised from acetone (Found: C, 25·55; H, 4·9%; *M*, ebullioscopic in 1% benzene solution, 767. $C_{18}H_{42}Br_4P_2Pd_2$ requires C, 25·3; H, 5·0%; *M*, 853). In a similar experiment in which acetone was used as solvent and the solution was not boiled but instead was kept at room temperature for 24 hr., a mixture of $(PPr^n_3)_2PdBr_2$ and $(PPr^n_3)_2Pd_2Br_4$ resulted. This was separated by extracting the former from the latter with light petroleum (b. p. 80—100°).

*Bis(tri-*n*-propylphosphine)di-iodo-μμ'-di-iododipalladium*, $[(PPr^n_3)_2Pd_2I_4]$.—Lithium iodide (18 g.) in acetone (100 c.c.) and hydrated sodium tetrachloropalladite (10 g.) in acetone (100 c.c.) were mixed, and tri-*n*-propylphosphine (4·3 g.) added under nitrogen. After 18 hr. the solution was taken to dryness at 15 mm. and the residual product was washed with methanol and dried. It was a mixture of $[(PPr^n_3)_2PdI_2]$ and $[(PPr^n_3)_2Pd_2I_4]$. The former was extracted with light petroleum (b. p. 80—100°), and the residue, recrystallised from chloroform, yielded iodine-like crystals (3·5 g.) of the desired *product* (Found: C, 20·9; H, 4·05. $C_{18}H_{42}I_4P_2Pd_2$ requires C, 20·8; H, 4·1%).

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451. *The Preparation and Properties of Some Pyrazolylacetic Acids.*

By E. G. BRAIN and I. L. FINAR.

Some pyrazoles containing the acetic acid side-chain have been prepared by means of the Willgerodt reaction, and their activity in the wheat cylinder test has been investigated.

ETHYL 3-ACETYL-4-METHYLPYRAZOLE-5-CARBOXYLATE [1] (I) was subjected to the Kindler [2] modification of the Willgerodt reaction employing sulphur and morpholine,[3] but the product was uncrystallisable. Attempts to isolate an acid from this by hydrolysis failed, but a crystalline thionmorpholide hydrochloride (II) was obtained and hydrolysed to the corresponding acetic acid (III). The same acetic acid derivative was obtained from 3-acetyl-4-methylpyrazole-5-carboxylic acid (IV): the mixture resulting from the action of sulphur and morpholine on this compound was water-soluble, and the thionmorpholide acid (V) was obtained as a solid on acidification. This also yielded the acid (III) on hydrolysis.

Methylation of the ester (I) gave only the 3-acetyl compound and none of the 5-acetyl isomer (VI*a*), as was shown by hydrolysis to a sterically hindered acid (VII) which was only slowly esterified by methanolic hydrogen chloride. The Willgerodt reaction with (VI) gave a crystalline 5-ethoxycarbonyl-1 : 4-dimethyl-3-pyrazolyl(thioacetmorpholide) (VIII) which was hydrolysed to the acetic acid derivative (IX).

Decarboxylation of the acid (VII) yielded a ketone (X), but the Willgerodt reaction on this failed to give the desired 1 : 4-dimethyl-3-pyrazolylacetic acid (XI). This acid, however, was obtained as its methyl ester (XIII) by decarboxylating the monomethyl ester (XII).

The Willgerodt reaction on 3-acetyl-4-methylpyrazole (XIV), followed by treatment of

[1] Klages, *J. prakt. Chem.*, 1902, **65**, 387.
[2] Carmack and Spielman, "Organic Reactions," Wiley, New York, 1946, Vol. III, p. 85.
[3] Schwenk and Papa, *J. Org. Chem.*, 1946, **11**, 798.

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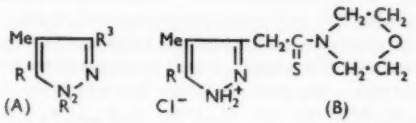
the product with hydrochloric acid, yielded a crystalline 4-methyl-3-pyrazolyl(thioacetmorpholide) hydrochloride (XV) which, on hydrolysis, gave the 4-methyl-3-pyrazolylacetic acid (XVI) in poor yield.



		R¹	R²	R³
I	A	CO_2Et	H	Ac
II	B	CO_2Et		
III	A	CO_2H	H	$CH_2·CO_2H$
IV	A	CO_2H	H	Ac
V	A	CO_2H	H	$CH_2·CS·N<C_4H_8>O$
VI	A	CO_2Et	Me	Ac
VIa	A	Ac	Me	CO_2Et
VII	A	CO_2H	Me	Ac
VIII	A	CO_2Et	Me	$CH_2·CS·N<C_4H_8>O$

		R¹	R²	R³
IX	A	CO_2H	Me	$CH_2·CO_2H$
X	A	H	Me	Ac
XI	A	H	Me	$CH_2·CO_2H$
XII	A	CO_2H	Me	$CH_2·CO_2Me$
XIII	A	H	Me	$CH_2·CO_2Me$
XIV	A	H	H	Ac
XV	B	H		
XVI	A	H	H	$CH_2·CO_2H$

The acids, as sodium salts, were subjected to the wheat cylinder test, the percentage elongations of wheat coleoptiles in solutions of the sodium salts being given in the Table. The compounds showed slight activity at concentrations rather close to those causing toxicity. In the pea curvature test all the acids were inactive at concentrations up to 500 p.p.m.

Elongation (%) of wheat coleoptiles in solutions of sodium salts of the pyrazolylacetic acids.

	Compound			
Concn. (p.p.m.)	III	IX	XI	XVI
0·1	100	102	99	99
1·0	100	102	104	102
10	104	101	102	102
100	115	102	102	109
500	Toxic	106	130	Toxic

Experimental

Orientation of 3-Acetyl-1 : 4-dimethylpyrazole-5-carboxylic Acids.—The total crude product (17·5 g.) obtained by methylating and then hydrolysing 3-acetyl-4-methylpyrazole-5-carboxylic ester [4] (19·6 g.) was refluxed for 3 hr. with 1% methanolic hydrogen chloride (500 g.), and the solution then rapidly evaporated. The residue was dissolved by shaking it with ether and aqueous sodium hydrogen carbonate. Unchanged acid was liberated from the aqueous solution with acid (14·5 g., 83%). The ethereal layer was evaporated, the residue hydrolysed, and the acid isolated (3·0 g., 17%). This acid was refluxed for 3 hr. with 1% methanolic hydrogen chloride (100 g.), and the unchanged acid separated from the ester by the above process (unchanged acid, 1·1 g., 37%; ester, 1·4 g., 45%); the ester (from dilute alcohol) melted at 157—158°, or at 155—156° when mixed with authentic methyl 3-acetyl-4-methylpyrazole-5-carboxylate (m. p. 155—157°) (Klages [4] gives m. p. 152°).

The recovered acid (14·5 g.) was refluxed for 3 hr. with 1% methanolic hydrogen chloride (400 g.), and the extraction repeated as before. The unchanged acid had m. p. 189—191° (Klages [4] gives 185—186°) (11·0 g., 76%). The methyl ester was obtained as needles, m. p. 110—111° (1·5 g., 97%).

Willgerodt Reaction of Ethyl 3-Acetyl-1 : 4-dimethylpyrazole-5-carboxylate. 5-Ethoxycarbonyl-1 : 4-dimethyl-3-pyrazolyl(thioacetmorpholide).—Ethyl 3-acetyl-1 : 4-dimethylpyrazole-5-carboxylate [4] (m. p. 85—86°; 5·0 g., 0·024 mole), sulphur (1·1 g., 0·033 g.-atom), and morpholine (7 c.c.; excess) were refluxed for 1 hr. at 150°. After cooling, the solidified mass was triturated with water, then dilute hydrochloric acid, then again water, and recrystallised from methanol (yield 3·72 g., 50%). The *morpholide* is obtained as pale cream needles, m. p. 103—104°, on rapid cooling, or as rhombs or platelets, m. p. 107—108°, by keeping the needles

[4] Klages and Rönneburg, *Ber.*, 1903, **36**, 1128.

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in contact with the mother-liquor for several days (Found : C, 53·7; H, 6·9; N, 13·8; S, 10·5. $C_{14}H_{21}O_5N_3S$ requires C, 54·0; H, 6·8; N, 13·5; S, 10·3%). Suspensions of the two forms in Nujol had different infrared absorption spectra but the spectra of 5% solutions in carbon tetrachloride were identical. 5-Ethoxycarbonyl-1 : 4-dimethyl-3-pyrazolyl(thioacetmorpholide) (5 g.) was refluxed for 5 hr. with 10% ethanolic potassium hydroxide (75 c.c.). Water (100 c.c.) was then added and the mixture evaporated to 50 c.c. to remove morpholine. 3N-Hydrochloric acid (50 c.c.) was next added and the mixture again evaporated to 50 c.c. (to remove hydrogen sulphide). On cooling (charcoal), the *pyrazolylacetic acid* crystallised as white needles (2·6 g., 82%), m. p. 197° (Found : C, 49·1; H, 5·3; N, 13·8. $C_8H_{10}O_4N_2$ requires C, 48·6; H, 5·1; N, 14·15%).

Willgerodt Reaction of Ethyl 5-Acetyl-4-methylpyrazole-3-carboxylate.—The procedure followed was as above, but the product could not be obtained solid, and no product could be obtained on hydrolysis. Treatment of the product from 4·0 g. of ester with concentrated hydrochloric acid (10—15 c.c.) gave a clear solution from which, on cooling, yellow crystals of *ethoxycarbonylmethylpyrazolyl(thioacetmorpholide) hydrochloride*, m. p. 158—161°, were obtained after washing with hydrochloric acid (3—5 c.c.) and drying *in vacuo*. Recrystallisation from chloroform–benzene gave crystals, m. p. 160—161° (Found : S, 9·9; Cl, 10·8. $C_{13}H_{20}O_3N_3ClS$ requires S, 9·6; Cl, 10·65%).

5-Carboxy-4-methyl-3-pyrazolylacetic Acid.—3-Ethoxycarbonyl-4-methyl-3-pyrazolyl(thioacetomorpholide) hydrochloride (1 g.) was refluxed for 3 hr. with 3N-aqueous sodium hydroxide. After cooling, some yellow amorphous material was filtered off. The solution was acidified and white needles of the *pyrazolylacetic acid*, m. p. 245—258°, formed in spherical agglomerates after 2—3 days. After two recrystallisions from hot water the m. p. was 265—267° (Found : C, 45·7; H, 4·55; N, 15·0. $C_7H_8O_4N_2$ requires C, 45·7; H, 4·4; N, 15·2%).

5-Carboxy-4-methyl-3-pyrazolyl(thioacetmorpholide).—The Willgerodt reaction on 5-acetyl-4-methylpyrazole-3-carboxylic acid (4·2 g.) yielded a water-soluble resin. A solution of this in water (100 c.c.) was slowly acidified (stirring) with dilute hydrochloric acid. The *morpholide* separated as a yellow precipitate, m. p. 235—236° (decomp.), but could not be recrystallised from the usual solvents; purified by reprecipitation (hydrochloric acid) from aqueous sodium hydrogen carbonate, it had m. p. 235—236° (decomp.) (Found : C, 48·8; H, 5·3; N, 15·8; S, 11·9. $C_{11}H_{15}O_3N_3S$ requires C, 49·0; H, 5·6; N, 15·6; S, 11·9%).

This morpholide (3 g.) was hydrolysed as described above. The carboxymethylpyrazolylacetic acid crystallised slowly from water in pale yellow rosettes, m. p. 264—266° (1·9 g., 91%). Recrystallisation from ethanol gave white crystals, m. p. 265—267°.

3-Acetyl-1 : 4-dimethylpyrazole.—3-Acetyl-1 : 4-dimethylpyrazole-5-carboxylic acid (15 g.) was heated at 240° ± 10° until vigorous ebullition ceased. The crude *acetyldimethylpyrazole* (10·4 g.) was then rapidly distilled off under reduced pressure and redistilled at 0·1 mm., the fraction boiling at 63—65° being collected (8·7 g., 76·5%). This solidified at 19—20° (Found : C, 60·9; H, 7·1; N, 20·0. $C_7H_{10}ON_2$ requires C, 60·8; H, 7·3; N, 20·3%).

Methyl 5-Carboxy-1 : 4-dimethylpyrazole-3-acetate.—5-Carboxy-1 : 4-dimethylpyrazole-3-acetic acid (1·55 g.) was refluxed for 3 hr. with 1% methanolic hydrogen chloride (250 c.c.), then evaporated to dryness, dissolved in aqueous sodium hydrogen carbonate, and extracted with ether. The aqueous solution was acidified and the *monoester* (1·5 g., 90%) filtered off; it had m. p. 141—142° (Found : equiv., 216. $C_8H_{11}O_2N_2{\cdot}CO_2H$ requires equiv., 212).

Methyl 1 : 4-Dimethyl-3-pyrazolylacetate.—Methyl 5-carboxy-1 : 4-dimethylpyrazole-3-acetate (2·0 g.) was heated at 200—240° for 1 hr. The product was distilled at 0·05—0·08 mm. and the fraction boiling at 76—78° was collected; this remained an oil (1·1 g., 70%).

1 : 4-Dimethyl-3-pyrazolylacetic Acid.—The preceding ester (1·0 g.) was saponified with ethanolic potassium hydroxide for 1 hr., and the solution was acidified, diluted with water, and extracted with chloroform. The extract was dried (Na_2SO_4) and evaporated; the residual solid, twice recrystallised from benzene–light petroleum and finally from benzene, had m. p. 107—109° (0·45 g.; 49%) (Found : C, 54·7; H, 6·6; N, 17·8. $C_7H_{10}O_2N_2$ requires C, 54·6; H, 6·6; N, 18·2%).

4-Methyl-3-pyrazolyl(thioacetmorpholide) Hydrochloride.—Crude 4-methyl-3-acetylpyrazole [4] (6·75 g.; m. p. 97—100°) was subjected to the Willgerodt reaction as in previous experiments but, after the reaction, excess of morpholine was removed at 120—130° under reduced pressure. To the remaining resin was added concentrated hydrochloric acid (10—20 c.c.) until it gave a paste of pale yellow crystals of the *morpholide hydrochloride*. This was cooled and filtered, and

the solid was washed with a small amount of concentrated hydrochloric acid, then dried on porous tile (yield, 7 g., 43%). Recrystallisation from ethanol gave white crystals, m. p. 206° (decomp.) (Found: N, 15·9; S, 12·15; Cl, 13·2. $C_{10}H_{16}ON_2ClS$ requires N, 16·0; S, 12·25; Cl, 13·6%).

4-Methylpyrazolyl-3-acetic Acid.—The preceding salt (7 g.) was hydrolysed by the normal method, but the aqueous solution, after filtration, was evaporated at 130°/20 mm. The dry residue was extracted with boiling ethanol, and the extract evaporated. The resinous residue (4·5 g.) was dissolved in aqueous sodium hydrogen carbonate, and the solution washed with benzene. The aqueous solution was acidified and extracted with ether (10 × 100 c.c.). The combined extracts gave a white crystalline residue on evaporation (0·4 g.), but further ether extracts yielded only negligible amounts of residue. The solid, after recrystallisation from benzene, consisted of white needles of the *4-methylpyrazolyl-3-acetic acid*, m. p. 116—117° (0·22 g.) (Found: C, 51·8; H, 5·9; N, 20·2. $C_6H_8O_2N_2$ requires C, 51·5; H, 5·7; N, 20·0%).

We thank Mr. H. Taylor of Wye College for the biological testing of our compounds. One of us (E. G. B.) thanks the D.S.I.R. for a maintenance grant.

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452. *The Effect of Peptising Agents on the Crystal Growth of Insoluble Metal Salts. Part II.*[1] *The Reduction of Particle Size of Crystalline Insoluble Metal Salts (and Sol Formation) by Surface-active Agents.*

By A. PACKTER.

The effect of macromolecules and colloidal electrolytes on the precipitation of crystalline insoluble metal salts from supersaturated solutions has been studied. The rate of fitting of the coagulated sol micelles into an ordered crystal structure is decreased more than the actual rate of coagulation: the appearance of the new phase of supersaturated solution is retarded, and the average particle size is reduced. The particle mass varies as an exponential function of the reciprocal of the concentration of peptiser. The results are best explained by the theory that peptisation occurs by adsorption of the added agent as a protective film round the sol micelles from which the crystals grow.

THIS paper extends a previous study [1] on the effect of organic acid peptising agents on the crystal growth of insoluble metal salts from supersaturated solution; the effect of addition of surface-active macromolecules and colloidal electrolytes has been investigated in greater detail.

EXPERIMENTAL

Materials.—Gelatins were supplied by the British Gelatine Works. The "Photographic" variety was freed from electrolytes and amino-acids by treatment with ion-exchange resins. The "free acidities" (*i.e.*, carboxyl groups including amino-acids formed by hydrolysis) expressed as c.c. of N-solution per 100 g. were: "Photographic" 14·9; "Coignet" 24·4; "Spa" 40·4 (cf. ref. 2).

Polysaccharides were supplied by B.D.H. Ltd. (of >95% purity).

Anionic and cationic colloidal electrolytes were prepared as described previously.[3]

Polyethylene glycol derivatives were supplied by General Metallurgical Co. Ltd.; polyethylene oxide derivatives by Dr. R. Matalon (for preparation see ref. 4).

Techniques.—An aqueous solution of the reacting cation (at 20°) was added to an equal volume of the reacting anion solution containing the required concentrations of peptising agent.

[1] Part I, Packter, *J.*, 1956, 2393.
[2] Matalon and Packter, *J. Colloid Sci.*, 1955, **10**, 46.
[3] Packter, *ibid.*, 1956, **11**, 150.
[4] Schulman, Matalon, and Cohen, *Discuss. Faraday Soc.*, 1956, **11**, 117.

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Sol Stability.—The stability of the supersaturated metal-salt systems was determined as described earlier,[1, 5] and the effects of the additives were followed up to the peptisation ratio.

Average Particle Size.—The precipitate was left to grow for 24 hr. at 20°. In the systems investigated in this work, the addition of peptising agent generally led to a fully deflocculated metal-salt sol or a suspension of average particle size within the range <0·05—5 μ: the average crystal diameter (d_c) (by weight) of the primary particles was been determined on the unfiltered deflocculated system, by the centrifugal sedimentation methods of Martin [6] and Jacobsen.[7]

Average Particle Weight.—The mean weight (m_c) of the primary particles will be given by the relation, $m_c = C\rho d_c^3$, where ρ is the specific gravity, and C is a shape factor.

Results

Stability.—We have shown previously [1, 5] that mixing the two reacting solutions generally causes an induction period (t) before the rapid onset of turbidity. This period t varies with the concentration (C_p) of peptiser, according to the general relation

$$\log_{10} t = F(C_p - \overline{C}_p)/C_s \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (1)$$

where $C_p = \overline{C}_p$ at $t = 1$ sec., and F is a constant.

C_p and C_s are generally expressed in g.-equiv. per l. F is always positive irrespective of whether the final crystal size of the metal-salt "deposit" is increased or reduced. If $C_p/C_s = (C_p^*/C_s)_t$ at $t = 24$ hr., $(C_p^*/C_s)_t$ is called the "peptisation ratio."

We have found that the F values for peptisation by macromolecules are generally 2—10 times less than those for peptisation by the corresponding monomer, while the $(C_p^*/C_s)_t$ values are larger. When, on the other hand, C_p and C_s values are expressed in moles per l., the values of the constant F may be >10,000 times greater than those for the corresponding monomer.

Size of Deposited Particles.—The crystallinity of many insoluble metal salts is markedly reduced when they are deposited in the presence of surface-active additives. Particles of colloidal size (deposited from solution) are in turn stabilised against coagulation and subsequent aggregation,[8-10] and concentrated insoluble metal-salt sols are formed.[11-13]

We have followed the variation of the particle size d_c, and of particle mass m_c, of such sols with concentration (C_p) of the peptising agent. As C_p is increased, d_c falls continuously from d_0* to below 0·05 μ, *i.e.*, m_c is reduced while N_c (the crystal number) is increased. For all the systems examined,

$$\log_{10}(N_o/N_c) = \log_{10}(M_c/M_o) = \log_{10}(d_c^3/d_o^3) = F'(C_p/C_s) \quad . \quad . \quad . \quad (2)$$

where $N_c = N_o$, $M_c = M_o$, and $d_c = d_o$ at $C_p = 0$. F' is a negative constant, equal to the value of $\log_{10}(M_c/M_o)$ at $C_p/C_s = 1$.

For the series of additives examined, $-F'$ values were generally equal between 0·3 and 0·8F.

The effect of all the peptising agents studied extends up to C_p values far beyond those that lead to minimum surface tension of the supersaturated solution.

Factors determining F' Values.—F' values in turn depend on the sol concentration, the structure of the peptising agent, and the solubility of the precipitated salt.

(a) *Variation with sol concentration.* For any system of metal-salt and peptising agent, $-F'$ falls markedly with increasing C_s values, according to a relation [5] of the type

$$-F' = \alpha(1/c_s)^m \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (3)$$

where α and m are constants. Some typical results are in Table 1.

* The particle size (d_c) of crystalline insoluble metal salts is generally >1 μ.

[5] Packter and Matalon, *Discuss. Faraday Soc.*, 1955, **18**, 161.
[6] Martin, *Ind. Eng. Chem. Anal.*, 1939, **11**, 471.
[7] Jacobsen and Sullivan, *Ind. Eng. Chem.*, 1946, **18**, 360.
[8] Odén, *Arkiv Kemi, Mineralog., Geol.*, 1926, **9**, 1.
[9] Kolthoff and Rosenblum, *J. Amer. Chem. Soc.*, 1934, **56**, 1264, 1658.
[10] Kolthoff and Eggertsen, *ibid.*, 1940, **62**, 2125.
[11] Tabory and Salvinien, *Bull. Soc. chim. France*, 1944, **11**, 431.
[12] Coribet and Hamdiken, *J. Chim. phys.*, 1954, **51**, 18.
[13] Moillet and Curie, "Surface Activity," Chapter 7, Spon Ltd., London, 1951.

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TABLE 1. *Variation of $-F'$ with sol concentration.*

System	$-F'$ at sol molarity stated 1/200	1/280	1/400	1/600	1/800	1/1000	1/2000
Ag_2CrO_4–gelatin (pH 3·6)	<0·1		0·3			0·65	
Ag_2CrO_4–Na_4 ethylenediamine-*NNN'N'*-tetra-acetate (pH 8·0)	0·7		1·8			8·6	64·0
Cu pyridine thiocyanate–gelatin (pH 6)			<0·05	0·10	0·30		
PbI_2-agar agar (pH 7; 30°)	6	19	90				

(b) *Variation with structure of the peptising agent.* Typical results for the peptising power (as measured by $-F'$) of series of colloidal electrolytes and macromolecules for different metal-salt systems at 20° are presented in Table 2.

TABLE 2. *Variation of $-F'$ with the nature of the peptising agent.*

M/400-Ag *salts*

Peptising agent	pH	$-F'$ Chromate	Oxalate
Gluconate	8·0	<0·01	<0·01
Citrate	8·0	0·032	0·01
Na_4 edta [a]	8·0	0·32	0·11
Gelatins :			
Coignet	3·6	0·60	0·30
Photogr.	3·6	0·50	0·25
Spa	3·6	0·80	0·30
Starch [b]	7·0	<0·05	n.d. [d]
Gum tragacanth [c]	7·0	0·16	,,
Alginate [c]	7·0	0·4	,,
Agar (at 30°) [d]	7·0	3·2	,,
$C_{12}H_{25}·SO_4Na$	Pptn. of Ag salt		
Na oleate	Pptn. of Ag salt		
Cetyl pyridinium bromide	Pptn. of Ag salt		
$HO·[(CH_2)_2·O·(CH_2)_2]_{10}·OL$ [f]	0·016	0·010	

M-600-Ca oxalate

Peptising agent	pH	$-F'$
Gelatin, photogr.	3·6	0·05
Agar	7·0	0·20
$H_p·[O·CH_2·CH_2]_n·OH$ [b]	7·0	0·90

M/600 Cu *pyridine thiocyanite*

Peptising agent	pH	$-F'$
Gelatins :		
Coignet	6·1	0·15
Photogr.	6·1	0·10
Starch	7·0	<0·05
Gum tragacanth	7·0	<0·05
Agar	7·0	0·50

M/200-Pb *salts*

Peptising agent	pH	$-F'$ Basic chromate	Iodide
Sucrose [d]	—	<0·05	<0·05
Dextrin [d]	—	<0·05	<0·05
Starch [d]	—	0·05	0·04
Methylcellulose	—	0·10	0·30
Gum tragacanth	7·0	3·0	2·8
CMC [e]	7·0	5·0	5·0
Agar (at 30°)	7·0	0·5	1·0
$H_p·[O·CH_2·CH_2]_n·OH$ [b]			
$n = 10$		n.d. [d]	0·006
$n = 15$		,,	0·007
$n = 23$		,,	0·008
$HO·[(CH_2)_2·O·(CH_2)_2]_n·OL$ [f]			
$n = 5$		,,	0·04
$n = 10$		,,	0·06
$n = 20$		,,	0·04

[a] edta = ethylenediamine-*NNN'N'*-tetra-acetate. [b] Equiv. wt. = 90, *i.e.*, one HO–CO_2H group per gluconic acid residue.[2] [c] Equiv. wt. = 100, *i.e.*, as in (*b*). [d] Equiv. wt. = 2000, *i.e.*, one free SO_4 group per 10 galactose units (Packter, *J. Phys. Chem.*, 1955, **59**, 1140. [d] n.d. = not determined. *L* = laurate. [e] CMC = carboxymethylcellulose. [b] Hp = heptyl. [Equiv. wt. = (mol. wt.)/*n*.]

High $-F'$ values, corresponding to marked peptising properties, are observed when the additive possesses two essential structural features, *viz.*, a polar grouping through which adsorption may occur on to the surface of the sol particle, and a lyophobic section.

Both polypeptides and polysaccharic acids are effective peptising agents for silver salts, while polysaccharic acids and non-ionic detergents are suitable for lead salts.

The order of $-F'$ values for peptisation of silver-salt systems follows inversely that of the " gold numbers " for peptisation of gold sols.[15,16]

(c) *Variation with solubility of the peptised salt.* We have compared the F' values for the peptisation, by the same surface active agent, of series of crystalline salts of the same cation but different solubility. No correlation has been observed between F' values and the metal-salt solubility, either when the former have been compared for systems at constant sol concentration,

[14] Packter, unpublished work.
[15] Paul, Szper, and Szper, *Kolloid Z.*, 1938, **82**, 43.
[16] Williams and Chang, *J. Phys. Chem.*, 1951, **55**, 719.

or at constant supersaturation (cf. refs. 1 and 5). It appears that the peptising effects of a particular additive on a metal salt are determined by interaction with the whole molecule of the metal salt, and are not related to interaction of the metal cation with the peptising agent.

Colloidal Sol Formation.—It follows from equation (2) that, for any system of metal salt and peptising agent system, $\log_{10} d_c^3 = \log_{10} d_o^3 + F'C_p/C_s$.

In those systems where d_o is low, and $-F'$ is high, the particle size of the material deposited from solution may fall to $d_c^* = 0{\cdot}01$ μ, the lower size limit for colloidal systems.

If $d_c = d_c^*$ at $C_p = C_p^*$, we may define the term $(C_p^*/C_s)_d$ as the peptisation ratio for size reduction (cf. ref. 5).

We have only verified relation (2) down to d_c values of *ca.* 0·05 μ; but if we assume that it is obeyed down to $d_c = d_c^*$, it follows that

$$(C_p^*/C_s)_d = [3 \log_{10} (0{\cdot}01/d_o)]/F' \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (4)$$

$(C_o^*/C_s)_d$ then varies inversely as $\log_{10} d_o^3$ and F'. Generally, the (C_p^*/C_s) values with the sol concentration and the nature of the peptising agent for a particular system of metal salt and peptising agent are in the same relative order as the concentrations required for deflocculation alone,[14] *i.e.*, the factors that enhance deflocculation lead to reduction of size at higher concentrations of peptising agent.

Discussion

Polypeptides, polysaccharic acids, and polyhydroxylic non-ionic colloidal electrolytes are all good modifiers of crystal size; and their addition reduces the particle size of the deposits from supersaturated solutions of insoluble metal salts.

Stable sols (of average particle size <0·1 μ) may be prepared from "colloidal" insoluble metal salts by precipitation from supersaturated solutions in presence of suitable deflocculating agents,[11-14] or by actual dispersion of the dried precipitate. Certain "crystalline" insoluble metal salts may also be prepared as particles of size <0·1 μ, by precipitation from very concentrated highly supersaturated solutions, but the complete deflocculation of these systems would require correspondingly large amounts of peptiser. The experiments described in this work suggest that a satisfactory method for preparing stable sols of many crystalline insoluble metal salts is to mix more dilute reacting solutions in presence of a peptising agent that reduces the particle size of the material deposited as well as acting as a deflocculant.

Most studies on modification of crystal size of soluble metal salts by surface-active agents have led to the conclusion that it is due to (physical) adsorption of monolayers of the added agent on to the growing host crystal, generally through specific polar groups. This adsorption in turn reduces the rate of both nucleus formation and crystal growth.[17,18] It seems reasonable to suggest that a similar mechanism will explain the effect of surface-active agents on the crystal size of insoluble salt precipitates or sols.*

We suggest that such adsorption of added agents reduces the rates of both coagulation and fitting of the sol micelles to form the final crystal (cf. ref. 1). The latter process is apparently affected to a far greater extent (cf. refs. 21); and only a small number of micelles fit on to an ordered crystal structure in each of the particles deposited

* Earlier workers [19] suggested that crystal growth and coagulation may be significantly affected by diffusion factors; and one might expect these to be especially important in the systems studied in the present work, where the addition of peptising agents may increase the viscosity appreciably. However, Collins and Leinweber [20] recently showed that the particle size of insoluble metal-salt precipitates, over a wide range of viscosity, is not appreciably modified by diffusion, since the rates of both "nucleus" formation and growth on to nuclei are equally affected by viscosity.

[17] Packter, *J. Phys. Chem.*, 1955, **59**, 1140.
[18] Buckley, "Crystal Growth," Chapter 10, Chapman & Hall, London, 1951; Bunn, *Proc. Roy. Soc.*, 1933, *A*, **141**, 567; Wells, *Discuss. Faraday Soc.*, 1949, **5**, 197; Geydal, *J. Amer. Chem. Soc.*, 1956, **78**, 1803.
[19] Valeton, *Z. Kryst.*, 1923, **59**, 335; van Hook and Bruno, *Discuss. Faraday Soc.*, 1949, **5**, 112.
[20] Collins and Leinweber, *J. Phys. Chem.*, 1956, **60**, 389.
[21] Abkin and Lipatov, *Trudy Moskov. Tecknol. Inst.*, 1941, 108; Nathanson, *Doklady Akad. Nauk, S.S.S.R.*, 1950, **74**, 517.

from solution. The final number deposited will then be increased, and the average particle size will be reduced (cf. refs. 22). The particle size will then vary with the concentration of peptising agent according to the exponential relation, $\log_{10}(d_c^3/d_c^3) = F'(C_p/C_s)$, where F' is negative, and the values of $-F'$ will be roughly equal to half those of F, the corresponding constant in the exponential relation between sol stability and peptiser concentration.

Although our present data are insufficient for a detailed quantitative analysis, the results are in general agreement with these concepts. With the fall in hydrophilic character of a polymer macromolecule, the peptising power may fall with reduced adsorption affinity; on the other hand, increased length of the hydrophobic groups associated with an anchored polar group will lead to enhanced steric or sheathing effects. Hence, as the molecular weight of a series of polymers of similar type increases, $-F'$ will depend on two conflicting factors: for some materials, $-F'$ increases with molecular weight, while for others it reaches an optimum for some particular chain length. On the other hand, the F values for increase in stability generally fall rapidly with lower overall polarity of the peptising agent.

The peptising power of certain materials may also be reduced by association or aggregation of molecules. For colloidal electrolytes, micelles are formed at low concentrations, while units of macromolecules may also cohere strongly at interfaces;[23] the latter effect may, for example, be the cause for the poor peptising properties of starches compared with that of methylcellulose.

Conclusions.—The addition of complex peptising agents to supersaturated solutions of insoluble metal salts reduces the particle size of the precipitate deposited.

The peptisation effects probably occur by adsorption of monolayers of the additive through polar groups on to the surface of the growing metal-salt particles.

I thank Professor Sir Eric Rideal for his interest.

KING'S COLLEGE, LONDON. [*Received, August 27th,* 1956.]

[22] Duke and Brown, *J. Amer. Chem. Soc.*, 1954, **76**, 1443; Packter, 2nd Internat. Congr. on Surface-Activity 1957.
[23] Sir Eric Rideal, *J. Polymer Sci.*, 1955, **16**, 531.

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453. *Purines, Pyrimidines and Glyoxalines. Part V.* New Syntheses of Uracils and Orotic Acids.*

By M. R. ATKINSON, (MISS) M. H. MAGUIRE, R. K. RALPH, G. SHAW, and R. N. WARRENER.

Syntheses of a number of substituted uracils and orotic acids from *N*-ethoxycarbonyl derivatives of propiolamide, β-ethoxyacrylamide, and maleic anhydride have been developed. A method of decarboxylating orotic acid and its derivatives is described.

EARLIER papers in this series have been partly concerned with the synthesis of 5-cyanouracils by reaction of a primary amine with the ethoxy-derivative (I; R = CN). Replacement of the cyano-group in these pyrimidines by hydrogen may be effected by acid hydrolysis and decarboxylation of the resulting 5-carboxylic acid. Two examples are described in the Experimental section. Such methods, however, would not be applicable to cyanouracils bearing acid-labile substituents, in particular sugar residues, and, in an attempt to widen the scope of our pyrimidine syntheses, we considered alternative routes to 1-substituted uracils from simple precursors, possibly analogous to those which might conceivably arise in biochemical systems. We now report some preliminary experiments

* Part IV, *J.*, 1956, 4118.

leading to the synthesis of simple precursors of uracil and uracil-6-carboxylic acid (orotic acid) derivatives.

Propiolic anhydride reacted remarkably slowly with urethane under a variety of conditions, to give eventually the propiolamide (II) which was accompanied by two isomeric substances formed by addition of urethane to the amide (II), and presumably *cis-trans*-isomers or α- and β-adducts. The propiolamide reacted vigorously with aniline at room temperature, to give the linear anilinoacrylamide (III; R = Ph) which with dilute alkali readily afforded 1-phenyluracil (V; R = Ph), also obtained from 5-cyano-1-phenyluracil by hydrolysis and decarboxylation.

(I) $R{\cdot}C(:CH{\cdot}OEt){\cdot}CO{\cdot}NH{\cdot}CO_2Et$ $HC{\equiv}C{\cdot}CO{\cdot}NH{\cdot}CO_2Et$ (II)

(III) $R{\cdot}NH{\cdot}CH{:}CH{\cdot}CO{\cdot}NH{\cdot}CO_2Et$ $EtO{\cdot}CH{:}CH{\cdot}CO_2Et$ (IV)

Reaction of ethyl propiolate with the sodium derivative of urethane gave a readily separable mixture of the β-ethoxyacrylamide (I; R = H) and ethyl β-ethoxyacrylate (IV). The ethoxyacrylamide (I; R = H) with ammonia, methylamine, and aniline followed by dilute alkali readily gave uracil, 1-methyluracil, and 1-phenyluracil (V; R = H, Me, and Ph) respectively.

Synthesis of orotic acid (VI; R = H) and derivatives by our present methods required an oxaloacetylurethane or its equivalent. Oxaloacetic acid and urethane in the presence of phosphoryl chloride or acetic anhydride gave a good yield of *N*-ethoxycarbonylaminomaleic anhydride (VII), whose structure is confirmed by hydrogenation followed by hydrolysis to aspartic acid, and by its further reactions. The anhydride with ammonia gave almost quantitatively a compound, presumably the maleimide (VIII; R = H), which with dilute alkali gave 5-carboxymethylenehydantoin (IX; R = R′ = H); this compound was converted into orotic acid when warmed with alkali (cf. Mitchell and Nyc [1]). Similarly the anhydride with aniline and sulphanilamide gave maleimides (VIII; R = Ph and *p*-$H_2N{\cdot}SO_2{\cdot}C_6H_4$) which when heated with alkali gave the 3-substituted orotic acids (VI; R = Ph or *p*-$H_2N{\cdot}SO_2{\cdot}C_6H_4$). A phenylorotic acid, identical with our material, has been prepared by the reaction of phenylurea with diethyl oxaloacetate and hydrolysis;[2] the intermediate product, assumed to be the ethyl ester of phenylorotic acid, is undoubtedly the hydantoin ester (IX; R = Ph, R′ = Et) since Mitchell and Nyc [1] have shown that condensation of urea with diethyl oxaloacetate gave the hydantoin ester (IX; R = H, R′ = Et). The position of the phenyl group in these compounds was based on experiments by Bachstez who prepared several alkylorotic acids

Ultraviolet absorptions.

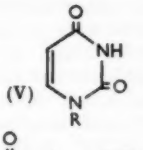
	(IX; R′ = Et)		(IX; R′ = H)		(VI)	
R	$\lambda_{max.}$ (mμ)	$10^{-3}\varepsilon$	$\lambda_{max.}$ (mμ)	$10^{-3}\varepsilon$	$\lambda_{max.}$ (mμ)	$10^{-3}\varepsilon$
H	300	13	290	11·8	278	6·4
Ph	278	12·6	282	15·2	280	6·7
Me	300	9·65	—	—	280	7·4

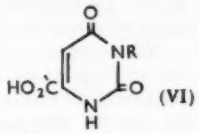
by the similar reaction of an alkylurea with diethyl oxaloacetate,[3] and the position of the substituent was assigned only by analogy with the reaction of alkylureas with ethyl acetoacetate. An alternative structure for the above-mentioned phenylorotic acid would be the carboxyhydantoin (IX; R = Ph, R′ = H). This compound has now been prepared from oxaloacetic acid and phenylurea and shown to differ from the phenylorotic prepared as above. In addition, the light absorption (see Table) of some orotic derivatives and analogous hydantoins clearly differentiates the two series, the hydantoins showing enhanced absorption.

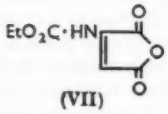
Final confirmation of the structures of both our phenyl orotic acid and the methylorotic acid prepared by Bachstez's method came by decarboxylation of the acids in

[1] Mitchell and Nyc, *J. Amer. Chem. Soc.*, 1947, **69**, 674.
[2] Ridi and Aldo, *Gazzetta*, 1952, **82**, 23.
[3] Bachstez, *Ber.*, 1931, **64**, 2683.

quinoline in the presence of copper powder to the known 3-phenyl- and 3-methyl-uracil. Orotic acid was also decarboxylated under these conditions to uracil. These appear to be the first recorded successful decarboxylations of orotic acid and its derivatives *in vitro*


(V)


(VI)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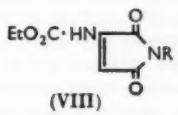
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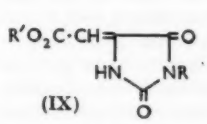
(IX)

although the biochemical decarboxylation of orotic acid is well known and of considerable importance.

Experimental

Unless otherwise indicated, compounds were dried for analysis at 55°/0·1—0·5 mm. over phosphoric oxide.

Reaction of Propiolic Anhydride with Urethane.—Propiolic anhydride[4] (7 g.) and urethane (5·1 g.) were heated together at 95° (internal temp.) for 2 hr. The product, which still contained excess of anhydride, was extracted with ether (100 ml.), and the extract washed with water (50 ml.) and 5% aqueous sodium hydrogen carbonate (2 × 50 ml.). The combined aqueous solutions were extracted with ether (50 ml.). From the dried ether solutions by evaporation was obtained a semicrystalline syrup which when treated with hot benzene left a *substance* (0·26 g.) which separated from chloroform as needles, m. p. 188° (Found: C, 46·8; H, 6·3; N, 12·25. $C_9H_{12}O_5N_2$ requires C, 46·95; H, 6·1; N, 12·2%). An *isomer* (0·7 g.) separated from the cooled benzene solution as prisms, m. p. 145° (Found: C, 47·1; H, 6·3; N, 12·3%). The benzene solution was finally evaporated and the residue distilled *in vacuo*, to give *N-ethoxycarbonylpropiolamide* (1·8 g.), b. p. 108—114°/4 mm., which crystallised, and recrystallised from benzene–light petroleum as laths, m. p. 74° (Found: C, 51·1; H, 5·05; N, 10·15. $C_6H_7O_3N$ requires C, 51·1; H, 5·0; N, 9·9%).

Reaction of Ethyl Propiolate with Sodium Urethane.—Urethane (5 g.) in ether (150 ml.) was heated under reflux with sodium (1·3 g.) for 5 hr. Ethyl propiolate (5·5 g.) in benzene (50 ml.) was added and the suspension was stirred and boiled under reflux for 60 hr. The resulting dark-brown solution was washed with ice-cold N-sulphuric acid (150 ml.); the aqueous phase was extracted with ether, and the combined ether solutions were dried and evaporated to an oil which was distilled *in vacuo*, to give fractions b. p. 40—80°/1 mm. and 120—126°/1 mm. The first fraction was redistilled and ethyl β-ethoxyacrylate (1 g.), b. p. 194°, was collected (Found: C, 58·1; H, 8·6. Calc. for $C_7H_{12}O_3$: C, 58·3; H, 8·4%). Deno[5] records b. p. 189—193°. The second fraction crystallised and after sublimation at 80—100°/0·1 mm. gave *β-ethoxy-N-ethoxycarbonylacrylamide* (1·6 g.), m. p. 84° (Found: C, 51·6; H, 6·9; N, 7·6. $C_8H_{13}O_4N$ requires C, 51·3; H, 7·0; N, 7·5%).

1-Phenyluracil.—(*a*) When *N*-ethoxycarbonylpropiolamide (0·12 g.) and aniline (0·08 g.) were mixed a vigorous reaction occurred. The cooled product crystallised and was triturated with ether, to give *β-anilino-N-ethoxycarbonylacrylamide* (0·16 g.) which separated from light petroleum (b. p. 60—80°) as cream-coloured prisms, m. p. 146—148° (Found: C, 61·1; H, 5·7; N, 12·0. $C_{12}H_{14}O_3N_2$ requires C, 61·5; H, 6·0; N, 12·0%). *N*-Ethoxycarbonylpropiolamide (0·16 g.) and aniline (0·11 g.) were treated as in the previous experiment; the product dissolved in 2N-potassium hydroxide (3 ml.) when shaken for a few min. Acidification gave a solid precipitate; *1-phenyluracil* (0·1 g.) separated from water as needles, m. p. 246° (Found: C, 63·7; H, 4·1; N, 14·75. $C_{10}H_8O_2N_2$ requires C, 63·8; H, 4·3; N, 14·9%). In

[4] Straus and Voss, *Ber.*, 1926, **59**, 1681.
[5] Deno, *J. Amer. Chem. Soc.*, 1947, **69**, 2233.

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admixture with 3-phenyluracil,[6] m. p. 244°, the compound had m. p. 210—220°. (*b*) 5-Cyano-1-phenyluracil [7] (2 g.) was boiled under reflux with 6N-hydrochloric acid (200 ml.) for 12 hr. The solution was concentrated to 50 ml., filtered hot, and cooled, a solid precipitate being obtained. This was washed with water, then kept with saturated aqueous sodium hydrogen carbonate (60 ml.) for 3 days. An insoluble sodium salt remained which was dissolved in water, and the solution acidified to give *1-phenyluracil-5-carboxylic acid* (0·4 g.) which separated from water as needles, m. p. 274° (decomp.) (Found: C, 57·2; H, 3·7; N, 12·6. $C_{11}H_8O_4N_2$ requires C, 56·9; H, 3·5; N, 12·1%). A sample was heated at the m. p. until effervescence ceased. The residue, crystallised from water, had m. p. 240° alone or mixed with 1-phenyluracil. Acidification of the sodium hydrogen carbonate solution precipitated unchanged 5-cyano-1-phenyluracil (0·2 g.), m. p. and mixed m. p. 280—283° (Found: C, 61·7; H, 3·6; N, 19·4. Calc. for $C_{11}H_7O_2N_3$: C, 61·95; H, 3·3; N, 19·7%). (*c*) β-Ethoxy-*N*-ethoxycarbonylacrylamide (0·05 g.) was gently warmed for 5 min. with aniline (0·35 ml.). The product was shaken with N-sodium hydroxide (1 ml.) on a water-bath for 5 min., and the excess of aniline removed by extraction with ether. Acidification of the aqueous solution gave a precipitate of 1-phenyluracil (0·05 g.), m. p. and mixed m. p. 244—245°. (*d*) Urethane (1·2 g.) was converted into the sodium derivative as in the above experiment. To the ethereal suspension was added ethyl propiolate (1·3 g.), and the mixture was boiled under reflux for 18 hr., cooled, washed with cold hydrochloric acid, dried, and evaporated to an oil. This was treated with aniline (1·25 ml.) and kept at 90° for 1 hr., and the resulting crystalline product shaken with 2N-sodium hydroxide (10 ml.) for 10 min. Excess of aniline was removed by extraction with ether, and the aqueous solution acidified with hydrochloric acid to give 1-phenyluracil (0·9 g.), m. p. and mixed m. p. 244°. Smaller yields of the same material were obtained when an excess of urethane was used or when the reactants were shaken together at room temperature for 16 hr. In the latter case a cleaner product was obtained initially.

Uracil and 1-Methyluracil.—(*a*) An ethereal solution of β-ethoxy-*N*-ethoxycarbonylacrylamide was prepared as under (*d*) above from urethane (2 g.). This was treated with 2N-aqueous ammonia (25 ml.), and the mixture evaporated to dryness at 60°. The residue was mixed with dilute sodium hydroxide solution and, after extraction with ether, acidified to give a precipitate of uracil (0·1 g.), m. p. and mixed m. p. 315—320°. (*b*) The intermediate prepared as in (*a*) from urethane (4 g.) was warmed with 33% ethanolic methylamine (5 ml.) at 60° for 20 min., then evaporated to dryness. The residue was warmed for 5 min. with 2N-sodium hydroxide (5 ml.), extracted with ether, and acidified. The solution was evaporated to dryness *in vacuo* and the residue extracted with *iso*butyl ketone (3 × 5 ml.); 1-methyluracil (0·2 g.) crystallised from the extract, having m. p. and mixed m. p. 233° (Found: C, 47·6; H, 4·8; N, 22·2; Calc. for $C_5H_6O_2N_2$: C, 47·6; H, 4·8; N, 22·2%). (*c*) 5-Cyano-1-methyluracil [7] (2·5 g.) was boiled under reflux with 6N-hydrochloric acid (15 ml.) for 8 hr. The solution was evaporated to dryness and the residue dissolved in aqueous sodium hydrogen carbonate. The acidified solution was extracted with ethyl acetate and from the organic phase was recovered *1-methyluracil-5-carboxylic acid* (1·8 g.) which recrystallised from water as prisms, m. p. 266° (decomp.) (Found: C, 42·1; H, 3·6; N, 16·5. $C_6H_6O_4N_2$ requires C, 42·4; H, 3·6; N, 16·5%). A small quantity of the acid was heated at 260—280° for 10 min.: it effervesced and a sublimate was obtained. This was resublimed at 150°/0·4 mm. to give 1-methyluracil, m. p. and mixed m. p. 231—232° (Found: N, 22·4%); Brown, Hoerger, and Mason [8] record m. p. 232—233°.

Reaction of Oxaloacetic Acid with Urethane.—Urethane (1·8 g.) and oxaloacetic acid (2·6 g.) in phosphoryl chloride (6 ml.) were heated at 70° until a clear solution was obtained (30 min.). This was cooled to give a crystalline precipitate which was filtered off and washed with ice-water (10 ml.). *N-Ethoxycarbonylaminomaleic anhydride* (2 g.) separated from ethyl acetate–light petroleum as needles, m. p. 118° (Found: C, 45·7; H, 4·1; N, 7·6. $C_7H_7O_5N$ requires C, 45·4; H, 3·8; N, 7·6%). The same compound was also obtained in lower yield by the reaction between urethane, oxaloacetic acid, and acetic anhydride. The anhydride (0·18 g.) in ethanol (20 ml.) was hydrogenated over platinum oxide for 3 hr., hydrogen absorption then ceasing. The solution was filtered and evaporated to dryness. The residue was boiled under reflux with N-hydrochloric acid (10 ml.) for 1 hr. Paper chromatograms of the solution were run, solvent being the upper layer of a mixture of butanol, water, and acetic acid (25 : 25 : 6).

[6] Whitehead, *J. Amer. Chem. Soc.*, 1952, **74**, 4267.
[7] Shaw, *J.*, 1955, 1834.
[8] Brown, Hoerger, and Mason, *J.*, 1955, 211.

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A strong ninhydrin-positive spot was obtained indistinguishable from that of aspartic acid run under identical conditions.

Orotic Acid.—The foregoing anhydride (0·3 g.) was dissolved in saturated ethanolic ammonia (5 ml.). After the initial spontaneous evolution of heat had ceased the solution was cooled to 0°; *N-ethoxycarbonylaminomaleimide* (0·28 g.) crystallised (m. p. 85°) (Found: N, 15·3. $C_7H_8O_4N_2$ requires N, 15·2%). The compound was unstable and deteriorated during several days at room temperature. The maleimide (0·51 g.) was dissolved in 2N-aqueous sodium hydroxide (3 ml.); the solution was warmed for 3 min. at 50°, cooled, and acidified to precipitate 5-carboxymethylenehydantoin (0·3 g.) which recrystallised from water as plates, decomp. from 300° (Found: C, 38·6; H, 2·7; N, 18·2. Calc. for $C_5H_4O_4N_2$: C, 38·5; H, 2·6; N, 17·95%); Mitchell and Nyc [1] record m. p. 300—400° (decomp.). As recorded by the latter authors, the hydantoin was readily converted into orotic acid. The hydantoin (10 mg.) was heated for 30 min. with N-potassium hydroxide (0·25 ml.), and the cooled solution acidified with hydrochloric acid to precipitate orotic acid monohydrate (9 mg.), m. p. 336° undepressed when admixed with a sample prepared from 6-methyluracil by Behrend and Struve's method.[9] Both compounds also moved as single spots (R_F 0·46) in propan-1-ol, formic acid, water (7 : 1 : 2).

3-Phenylorotic Acid.—(*a*) Aniline (0·1 g.) was added to a solution of the anhydride (0·17 g.) in ethanol (1 ml.). The solution was warmed for a few min. to give a yellow solution which when cooled gave a crystalline precipitate. *α-N-Ethoxycarbonylamino-N'-phenylmaleimide* (0·1 g.) crystallised from ethanol as needles, m. p. 135° (Found: C, 59·95; H, 4·95; N, 11·1. $C_{13}H_{12}O_4N_2$ requires C, 60·0; H, 4·65; N, 10·8%). Aqueous sodium hydroxide was added gradually to a suspension of the phenylmaleimide (1 g.) in water (3 ml.) to give a clear solution. This was cooled and acidified with 10N-hydrochloric acid, giving a crystalline precipitate; 3-phenylorotic acid monohydrate (0·64 g.) recrystallised from ethanol as needles, m. p. 280° (decomp. with loss of solvent from 180°) (Found: C, 53·1; H, 4·1; N, 11·15. Calc. for $C_{11}H_8O_4N_2,H_2O$: C, 52·8; H, 4·0; N, 11·2%). The compound was recovered unchanged after treatment with N-potassium hydroxide at 100° for 30 min. (*b*) The anhydride (0·5 g.) and aniline (3 ml.) were heated together for 10 min. at 60° and the product stirred with 2N-sodium hydroxide (2·5 ml.) for a further 10 min. Unchanged aniline was removed by extraction with ether and 3-phenylorotic acid monohydrate (0·31 g.) was recovered by acidification of the alkaline solution. The acid had m. p. and mixed m. p. 280° (decomp.) (Found: C, 52·9; H, 4·0; N, 11·2%). (*c*) To a solution of 5-carbethoxymethylene-3-phenylhydantoin (prepared from diethyl oxaloacetate and phenylurea) (1·44 g.) in boiling ethanol (100 ml.) was added a solution of potassium hydroxide (0·6 g.) in water (3 ml.). The yellow solution was cooled and treated with water (34 ml.), then evaporated *in vacuo* to a small volume. This, when acidified with hydrochloric acid, precipitated 3-phenylorotic acid monohydrate (1·25 g.) which separated from water as needles, m. p. and mixed m. p. 280° (decomp.).

5-Carboxymethylene-3-phenylhydantoin.—Dry hydrogen chloride was passed through a mixture of oxaloacetic acid (6·6 g.) and phenylurea (6·8 g.) in glacial acetic acid (50 ml.) for 30 min. at 80°. The solution was kept at 0° for 3 days, a solid separating. *5-Carboxymethylene-3-phenylhydantoin* (2·1 g.), crystallised from water, had m. p. 200° (decomp.) (Found: C, 56·8; H, 3·45; N, 12·15. $C_{11}H_8O_4N_2$ requires C, 56·9; H, 3·45; N, 12·05%). Hydrolysis of the acid with aqueous potassium hydroxide gave 3-phenylorotic acid.

Decarboxylation of 3-Phenylorotic Acid.—A solution of 3-phenylorotic acid monohydrate (0·84 g.) in quinoline (4 ml.) was boiled with copper powder (0·1 g.) for 1 hr. The cooled solution was treated with N-sodium hydroxide (20 ml.) and extracted with ether. The alkaline solution was acidified and cooled overnight, crystals separating. 3-Phenyluracil (0·34 g.) separated from water as needles, m. p. and mixed m. p. 246—247° (Found: C, 63·8; H, 4·45; N, 14·7. Calc. for $C_{10}H_8O_2N_2$: C, 63·8; H, 4·45; N, 14·9%). A mixed m. p. with 1-phenyluracil (m. p. 246°) was 210°.

Decarboxylation of Orotic Acid.—Orotic acid (0·18 g.) in quinoline (3 ml.) containing copper powder (0·03 g.) was boiled under reflux for 1 hr. The cooled solution was treated with 2N-sodium hydroxide (4 ml.) and water (2 ml.) and extracted with ether. The aqueous phase was acidified and continuously extracted with ethyl acetate. Evaporation of the solvent gave uracil (0·05 g.) which separated from water as needles, m. p. and mixed m. p. 330° (decomp.) (Found: N, 24·9. Calc. for $C_4H_4O_2N_2$: N, 25·0%). The compound was indistinguishable from uracil in a paper chromatogram run in butanol, formic acid, water (77 : 13 : 10) (R_F = 0·32).

[9] Behrend and Struve, *Annalen*, 1911, **378**, 153.

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Decarboxylation of 3-Methylorotic Acid.—5-Ethoxycarbonylmethylene-3-methylhydantoin was prepared from methylurea and diethyl oxaloacetate. The product had m. p. 135°. The hydantoin (1 g.) was heated with 2N-sodium hydroxide (10 ml.) for 30 min. at 100°. The cooled solution was acidified with 10N-hydrochloric acid, 3-methylorotic acid (0·7 g.), m. p. 300° (decomp.), being precipitated; this recrystallised from water (Found: C, 42·55; H, 3·55; N, 16·55. Calc. for $C_6H_6O_4N_2$: C, 42·35; H, 3·55; N, 16·45%). The acid was suspended in quinoline (4 ml.) containing copper powder (0·1 g.) and the mixture boiled for 45 min. The cooled solution was treated with 2N-sodium hydroxide (10 ml.) and extracted with ether. The aqueous phase was acidified and continuously extracted with ethyl acetate for 3 hr. Evaporation of the ester solution gave a solid residue. 3-Methyluracil (0·06 g.) separated from ethanol as needles, m. p. and mixed m. p. 179° (Found: N, 22·35. Calc. for $C_5H_6O_2N_2$: N, 22·2%).

3-p-*Sulphamoylphenylorotic Acid.*—*N*-Ethoxycarbonylaminomaleic anhydride (0·55 g.) and sulphanilamide (0·42 g.) were warmed together in ethanol (5 ml.) until a clear solution was obtained. The cooled solution gave a crystalline precipitate; α-N-*ethoxycarbonylamino*-N′-p-*sulphamoylphenylmaleimide* (0·3 g.) separated from ethanol as needles, m. p. 240° (decomp.) (Found: C, 45·9; H, 4·1; N, 12·2. $C_{13}H_{13}O_6N_3S$ requires C, 46·0; H, 3·9; N, 12·4%). The maleimide (0·6 g.) was dissolved in warm 2N-sodium hydroxide (3 ml.), and the solution acidified to give a solid precipitate. 3-p-*Sulphamoylphenylorotic acid* (0·28 g.) separated from water as hydrated needles, m. p. 320° (decomp.) (Found, in material dried at 100°/0·1 mm.: C, 41·9; H, 3·4; N, 13·15. $C_{11}H_9O_6N_3S,\frac{1}{2}H_2O$ requires C, 41·9; H, 3·3; N, 13·3%). Found, in material dried at 136°/0·1 mm.: C, 42·6; H, 3·2; N, 13·3. $C_{11}H_9O_6N_3S$ requires C, 42·4; H, 2·9; N, 13·5%).

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454. *The Thermal Decomposition of the Chlorofluoromethanes.*

By A. B. Trenwith and R. H. Watson.

The thermal decomposition of the three fluorochloromethanes has been studied in an alumina vessel between 400° and 900° and at pressures of about one atmosphere. Stability increases with the proportion of fluorine in the molecule. Interpretation of the results is rendered difficult by reactions involving the alumina surface at higher temperatures. It is clear, however, that in every case the principal products of homogeneous pyrolysis are compounds containing one fluorine atom more and one less than the parent halogenocarbon together with chlorine. Mechanisms have been suggested to account for the formation of these products and others obtained in smaller yield.

The chlorofluoromethanes are relatively unreactive. Ruff and Keim [1] found that they attacked sodium, barium, and magnesium at 600° and some of them at least react with other elements. Thus dichlorodifluoromethane has been shown, in these laboratories, to behave at 500° as a mild chlorinating agent towards tellurium, which is thereby converted into the dichloride.[2] Their thermal decomposition does not appear to have been studied and, as one of us has been associated with a corresponding investigation of tetrafluoroethylene,[3] it seemed useful to apply the methods there developed to these three

[1] Ruff and Keim, *Z. anorg. Chem.*, 1931, 201, 245.
[2] Aynsley, *J.*, 1953, 3016.
[3] Atkinson and Trenwith, *J.*, 1953, 2082.

compounds. Tetrafluoroethylene could be decomposed in a steel vessel without appreciable attack on the metal, but at the temperatures required to decompose the chlorofluoromethanes they were far too corrosive for metals or silica, and even the fused alumina eventually resorted to was not immune. This failure to find an inert reaction vessel has precluded a detailed study of the kinetics of the decomposition, but enough information has been gathered to yield a general picture of their thermal stability and mode of decomposition.

Experimental

Materials.—The chlorofluoromethanes (" arctons "), from Imperial Chemical Industries Limited, were received in cylinders.

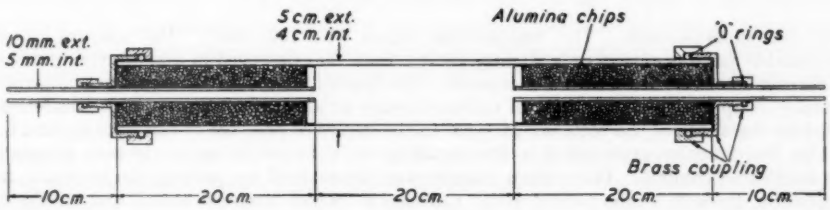
Chlorotrifluoromethane. The gas contained small amounts of carbon dioxide, oxygen, and nitrogen. The first was removed by passage through saturated aqueous potassium hydroxide followed by concentrated sulphuric acid; the second by means of a tower packed with activated copper on kieselguhr [4] at 200°; the nitrogen was ignored. Before use the gas was dried (P_2O_5).

Dichlorodifluoromethane. The carbon dioxide and oxygen were removed as before. A trace of high-boiling material was removed by passing the gas through a trap cooled to −29°.

Trichlorofluoromethane. This was condensed directly into the boiler of a Podbielniak-type fractionating column. After the removal of non-condensable matter by pumping, the condensable material was fractionated and a middle cut of the fraction boiling at 12°/500 mm. was retained for pyrolysis.

Apparatus.—This consisted of a purification train, a flow-meter, an alumina reaction vessel, collecting traps, a low-temperature Podbielniak-type distilling column and a bulb of accurately known volume for molecular-weight determinations. A mercury-vapour pump, backed by a rotary oil pump, was used to evacuate the apparatus which, except for the reaction vessel, was of Pyrex glass.

Several materials were tried for the reaction vessel. Silica was readily attacked giving silicon tetrafluoride and oxides of carbon, and metals gave volatile chlorides: only fused alumina proved satisfactory, and even this suffered some attack at the higher temperatures. Owing to the difficulty and cost of special fabrication in fused alumina, we were unable to have a normal form of reaction vessel and resorted to the method shown in the Figure whereby the centre portion of a fused alumina tube was converted into a reaction vessel by means of two circular plates of the same material. These fitted closely and had fused into them tubes which reached to the outside. Special adaptors were made to close both the wide and narrow tubes by means of compression rings. The reaction tube was heated in a tubular electric furnace controlled to ±1° by a " Sunvic " energy regulator. Temperatures were measured by means of a chromel–alumel thermocouple in a sheath between the reaction vessel and the furnace tube.



Operation.—Before use the surface of the reaction vessel was conditioned by treatment with fluorine (2%) in nitrogen at 650°. This eliminated surface reactions at temperatures below 700°. To retain as nearly as possible the same surface conditions throughout the investigation, the vessel was periodically opened and the surface rubbed with emery paper and reconditioned as before.

Chlorotrifluoromethane and dichlorodifluoromethane were passed through the purification

[4] Meyer and Ronge, *Angew. Chem.*, 1939, **52**, 637.

train and flow-meter and into the reaction vessel, the cylinder valve being adjusted to give a steady flow at a pressure very near 1 atm. In order to allow the reaction to settle down, the products of pyrolysis formed during the first 15 min. of each run were pumped off, and the rest were collected in two traps cooled in liquid nitrogen. At the end of a run the pressure of non-condensable gas in the system was noted and, when necessary, this gas was analysed. The condensable products were transferred to the low-temperature column and analysed by fractional distillation. Where there was ambiguity, fractions were identified by molecular-weight determination, and sometimes by chemical or mass-spectrometric analysis.

Since trichlorofluoromethane boils at 23° its vapour could not be conveniently handled in the system at 1 atm., so a pressure of 400 mm. was employed. The material was drawn from a small storage bulb attached to the purification train through a tap; by adjusting this and the temperature of the bulb a steady flow of gas at the prescribed pressure was maintained.

Results.—Dichlorodifluoromethane. The decomposition was studied over the range 700—900°. Up to 800° the non-condensable gas was entirely nitrogen of equal amount to that obtained in a blank run with an unheated reaction vessel. At 850°, in addition to nitrogen, the non-condensable gases contained a small amount of carbon monoxide and at 900° this was appreciably greater and some carbon dioxide was also found, indicating an attack on the walls which was slight at 850° and increased with temperature. The gas itself was quite stable below 750° and almost completely decomposed at 900°. The principal products were chlorotrifluoromethane and chlorine; in addition there were smaller amounts of trichlorofluoromethane, carbon tetrachloride, a high-boiling liquid, and a white solid. The high-boiling liquid (b. p. ~115°) was a mixture with a carbon : fluorine : chlorine atomic ratio of 3 : 6 : 2, but the white solid contained very little chlorine (~3·5% w/w). Analysis enabled a balance of the carbon, fluorine, and chlorine to be struck which demonstrated the absence of measurable attack on the vessel below 850°, the atomic ratio carbon : fluorine : chlorine being almost exactly 1 : 2 : 2. The small deficiency of carbon and fluorine noticed at 850°, which became more pronounced at 900°, was presumably due to the formation of aluminium fluoride and oxides of carbon. The analyses are given in Table 1.

TABLE 1. *Products of pyrolysis of dichlorodifluoromethane.*

CF_2Cl_2 passed/hr. = 1·5 l.; pressure in reaction vessel = 760 mm.

	Products (moles/100 moles of CF_2Cl_2 passed)								
Temp.	CF_4	CF_3Cl	CF_2Cl_2	$CFCl_3$	CCl_4	Cl_2	$C_2F_4Cl_2$	High-b. p. liquid	White solid *
700°	—	—	100	—	—	—	—	—	—
750	—	1·5	96·2	0·4	—	2·7	0·2	—	—
800	1·1	10·7	73·4	4·9	1·3	11·9	—	0·8	95 g.
850	1·5	33·1	23·2	6·9	7·5	34·6	—	5·0	110 g.
900	2·0	31·2	6·1	5·8	4·7	50·6	—	3·0	300 g.

* g./100 moles of CF_2Cl_2 passed.

Chlorotrifluoromethane. The temperature range was 700—850°. The amount of non-condensable gas was always only slightly greater than that observed in a blank run, indicating the formation of very little carbon monoxide. Analysis of the condensable products showed the presence of appreciable quantities of carbon dioxide at all temperatures. This was substantiated by the shape of the plateaux at −83° in the curves of pressure of distillate against b. p., and by the difficulty experienced in fractionating the mixtures owing to vigorous bumping in the distillation column. The carbon dioxide was determined by passing the products, after distillation, through a tube packed with " Carbosorb " which removed both it and the chlorine. Subsequent fractionations produced distillation curves with shorter and more clearly defined plateaux at −83°, the decrease in length always being equivalent to the amount of carbon dioxide originally present. Mass-spectrometric analyses showed that the distillates at −83°, after the removal of carbon dioxide, were pure chlorotrifluoromethane.

The results are given in Table 2. The figures given for carbon tetrafluoride throughout this paper are probably slightly low, since, owing to its high vapour pressure, some must inevitably have been lost when removing the non-condensable gas.

As the proportionally large quantities of carbon dioxide indicate appreciable attack on the reaction vessel at all temperatures, it seemed unprofitable to use temperatures above 850°.

Trichlorofluoromethane. The temperature range was 440—745°. The gas begins to decompose at about 400° and, under the experimental conditions, decomposition was practically complete at 745°. Some surface reaction at 650° and above was indicated by the appearance of carbon monoxide in the non-condensable matter. No carbon dioxide was found at any temperature. The principal products were chlorine, carbon tetrachloride, and dichlorodifluoromethane; they were accompanied by a small amount of high-boiling liquid which was a mixture.

TABLE 2. *Products of pyrolysis of chlorotrifluoromethane.*

CF_3Cl passed/hr. = 2·25 l.; pressure in reaction vessel = 760 mm.

	Products (moles/100 moles of CF_3Cl passed)				
Temp.	CF_4	CF_2Cl_2	CF_2Cl_4	CO_2	Cl_2
706°	—	99·6	—	0·3	0·2
748	—	95·4	—	4·1	2·3
797	0·1	84·4	0·2	14·4	7·7
850	0·9	66·1	3·5	29·3	14·6

An analysis of the materials produced at 745° showed that a little of the carbon was missing; this is ascribed to the decomposition of some of the carbon tetrachloride formed into carbon and chlorine. The results are given in Table 3.

TABLE 3. *Products of pyrolysis of trichlorofluoromethane.*

$CFCl_3$ passed/hr. = 2·25 l.; pressure in reaction vessel = 400 mm.

	Products (moles/100 moles of $CFCl_3$ passed)					
Temp.	CF_2Cl	CF_2Cl_2	$CFCl_3$	CCl_4	Cl_2	High-b. p. liquid
440°	—	1·6	96·8	1·6	—	—
498	—	6·4	87·3	6·4	trace	—
603	—	15·9	44·4	26·4	13·0	3·6
650	—	18·0	25·5	30·8	26·0	6·7
705	—	12·2	18·1	27·2	48·7	9·9
745	1·1	8·0	13·5	23·9	70·1	10·9

DISCUSSION

This study of the pyrolysis of the chlorofluoromethanes, which has been inevitably complicated, at the higher temperatures, by reactions involving the surface of the vessel, indicates that their modes of decomposition are inherently complex. Nevertheless, general conclusions can be reached.

The chlorofluoromethanes are particularly stable and the stability increases with the fluorine : chlorine ratio. Thus although trichlorofluoromethane begins to decompose at 400°, both dichlorodifluoromethane and chlorotrifluoromethane are stable below 700°. The dichlorodifluoromethane is less stable than chlorotrifluoromethane, for at 850° approximately 80% is decomposed as compared with 40% of the chlorotrifluoromethane under comparable conditions.

In the pyrolysis of dichlorodifluoromethane the products probably arise from an initial splitting of a carbon–chlorine bond followed by reactions of the chlorine atom and radical formed with parent molecules. Most of the chlorine produced would then result from the reactions,

$$CF_2Cl_2 \longrightarrow CF_2Cl\cdot + Cl\cdot \quad \ldots\ldots\ldots (1)$$

and

$$Cl\cdot + CF_2Cl_2 \longrightarrow CF_2Cl\cdot + Cl_2 \quad \ldots\ldots\ldots (2)$$

and other products could arise from two further reactions involving the transfer of either a fluorine or a chlorine atom from the parent molecule to a radical as shown :

$$CF_2Cl\cdot + CF_2Cl_2 \longrightarrow CF_3Cl + CFCl_2\cdot \quad \ldots\ldots\ldots (3)$$

$$CFCl_2\cdot + CF_2Cl_2 \longrightarrow CFCl_3 + CF_2Cl\cdot \quad \ldots\ldots\ldots (4)$$

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It is to be noted that where a fluorine-atom transfer is involved a chlorine-atom transfer can also be postulated and *vice versa*, but the alternatives will produce no net change in the system. Reactions (1)—(4) account for the three principal products of pyrolysis.

Above 700° chlorotrifluoromethane is unstable and trichlorofluoromethane even more so. Clearly the small amounts of secondary products may result from the subsequent decomposition of these primary ones. Thus decomposition of chlorotrifluoromethane could account for the small amounts of carbon tetrafluoride found and the carbon tetrachloride may result from that of trichlorofluoromethane. The formation of materials of high molecular weight may arise from radical recombination followed by the splitting off of a chlorine atom and further radical recombination (5—7). The trace of dichlorotetrafluoroethane produced at 750° indicates the occurrence of reaction (5) at this temperature, and the absence of this product at higher temperatures may be due to its low stability.

$$CF_2Cl\cdot + CF_2Cl\cdot \longrightarrow C_2F_4Cl_2 \quad \ldots\ldots\ldots\ldots (5)$$

$$C_2F_4Cl_2 \longrightarrow C_2F_4Cl\cdot + Cl\cdot \quad \ldots\ldots\ldots\ldots (6)$$

$$C_2F_4Cl\cdot + CF_2Cl\cdot \longrightarrow C_2F_5Cl_2 \quad \ldots\ldots\ldots\ldots (7)$$

From chlorotrifluoromethane, by analogy, we should expect the principal products to be carbon tetrafluoride, dichlorodifluoromethane, and chlorine, all of which were obtained. The proportion of carbon dioxide also formed at all temperatures showed, however, that reaction with the walls of the vessel was considerable.

The pyrolysis of trichlorofluoromethane is of more interest since, in this instance, surface effects are too slight to confuse the issue. A mechanism similar to that already suggested would lead to dichlorodifluoromethane, carbon tetrachloride, chlorine, and some high-boiling material together with smaller quantities of chlorotrifluoromethane and carbon tetrafluoride. All of these were found with the exception of the last. Although at all temperatures used chlorine is the major product from dichlorodifluoromethane, with trichlorofluoromethane this is not so below 650°. At 500°, for example, only dichlorodifluoromethane and carbon tetrachloride appear in measurable quantity, and even at 600° they both exceed the chlorine produced. There appear to be two possible explanations for these observations: the first invokes the straightforward bimolecular reaction

$$2CFCl_3 \longrightarrow CF_2Cl_2 + CCl_4$$

concurrent with, but predominant over, the free-radical reactions at the lower temperatures; the second calls for a chain process in which reactions similar to (3) and (4) are the chain-carrying steps. With dichlorodifluoromethane the high proportion of chlorine formed precludes such chain reactions but with trichlorofluoromethane at the lower temperatures this restriction does not operate. Unfortunately the evidence is insufficient to allow us to decide between these alternatives, but since there is little to suggest a bimolecular reaction in the case of either chlorotrifluoromethane or dichlorodifluoromethane we are led to prefer the latter.

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455. *Adsorption on Carbons from Binary Liquid Mixtures: Some Surface Activity Coefficients.*

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Surface activity coefficients are compared for a range of binary liquid mixtures adsorbed on charcoal. The curves of surface activity coefficient against surface mole-fraction are of three types, corresponding to the types of isotherm of concentration change and of individual adsorption isotherm. In general, there is no correlation between the surface activity coefficients and those for the corresponding liquid phase. Surface forces are the most important in most cases, though absolute volatility is also important and may become the over-riding factor in extreme cases. In a special series, charcoal shows a preference for the less polar methyl group over the more polar chlorine atom. A comparison is made of the behaviour of one system on charcoal, on carbon black, and on graphite.

The forces of physical adsorption which hold the molecules of a substance to a solid surface and prevent their return to the liquid or vapour phase have been likened to those holding together the molecules in the liquid phase, so preventing their escape into the vapour phase. When a binary mixture is involved, the adsorbate has, in general, a different composition from that of the liquid in equilibrium with it, just as the liquid usually has a different composition from that of its saturated vapour. It is interesting, therefore, to investigate the "surface activity coefficients" for such systems, *i.e.*, the activity coefficients of the two components in the adsorbed layer. These should show the relative tendencies of the two substances to escape from the surface.

Surface activity coefficients have been considered from a theoretical standpoint by Elton [1] for such systems. We now present the data obtained from a series of experimental investigations and use them to draw a number of simple qualitative conclusions about the forces responsible for adsorption.

Two conventions have been used for expressing surface activity coefficients. Elton's convention, which we shall follow, is that the surface activity of either component, and hence its surface activity coefficient, is 1 when its surface mole-fraction is 1. This convention seems particularly suited to a comparison of activity coefficients for the adsorbed layer and for the bulk liquid when completely miscible liquids are being considered. In particular, it is more appropriate than the convention used by Fu, Hansen, and Bartell [2] in dealing with partially miscible systems.

We have $f_1 = a_1/x_1$ and $f_1^s = a_1^s/x_1^s$ where f_1 and f_1^s are the activity coefficients of substance 1 in the liquid and the surface phase respectively, a_1 and a_1^s are the corresponding activities, and x_1 and x_1^s the corresponding mole-fractions. The surface mole-fractions are obtained from the individual adsorption isotherms, the derivation of which has been discussed previously.[3-6] With the present convention, $a_1 = a_1^s$ for any mixture. The value of a_1 is obtained from vapour-pressure measurements; hence values of f_1 and of f_1^s can be calculated. Calculations have been made for: (1) A series of mixtures adsorbed on charcoal, for which the individual isotherms have been recorded previously,[3-6] and (2) two further series, isotherms for which are recorded in this paper, in which (*a*) pairs are taken from the group carbon tetrachloride, chloroform, 1 : 1 : 1-trichloroethane (methylchloroform), *tert.*-butyl chloride [these substances have molecules of very similar size and shape, and it was hoped to derive information about the relative effects in adsorption of the chlorine atom, hydrogen atom, and methyl group], and (*b*) a comparison is made, for one

[1] Elton, *J.*, 1954, 3813.
[2] Fu, Hansen, and Bartell, *J. Phys. Colloid Chem.*, 1948, **52**, 374.
[3] Kipling and Tester, *J.*, 1952, 4123.
[4] Blackburn and Kipling, *J.*, 1954, 3819.
[5] *Idem*, *J.*, 1955, 1493.
[6] *Idem*, *J.*, 1955, 4103.

liquid mixture, of adsorption on the porous charcoal used throughout this work with adsorption on a non-porous carbon black, and on a non-porous graphite.

The results of adsorption measurements which have not been published previously are shown in Figs. 1—4. The individual adsorption isotherms have been calculated as described previously [3,4] from the monolayer values recorded in the Tables; from these were obtained the values of x_1^s and x_2^s. The partial-pressure data are recorded, for convenience, in the form of activity coefficients, together with the vapour pressures of the pure components.

FIG. 1. *Isotherms of concentration change for adsorption from mixtures of benzene and* cyclo*hexane on* (○) *Spheron* 6, (●) *graphite.*

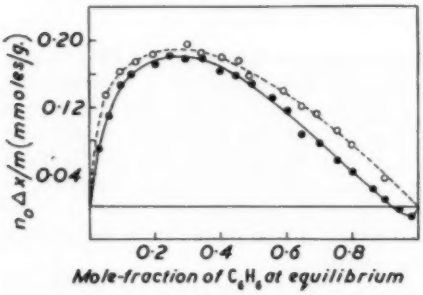


FIG. 2. *Isotherms of concentration change for adsorption on charcoal from mixtures of* (*a*) *methylchloroform* (*A*) *and* tert.*-butyl chloride,* (*b*) *methylchloroform* (*A*) *and carbon tetrachloride,* (*c*) tert.*-butyl chloride* (*A*) *and carbon tetrachloride,* (*d*) *chloroform* (*A*) *and carbon tetrachloride.*

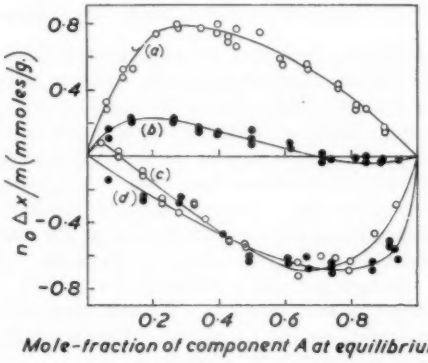


FIG. 3. *Isotherms of concentration change for adsorption on charcoal from mixtures on* (*a*) n*-butylamine and benzene,* (*b*) *methyl acetate and benzene.*

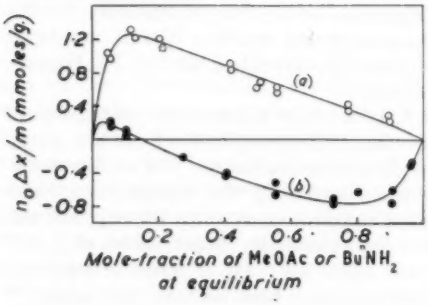
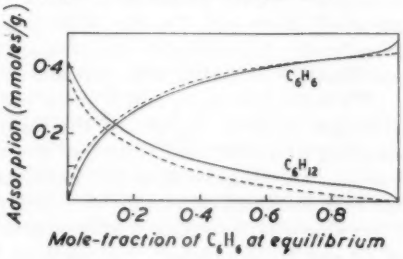


FIG. 4. *Adsorption (individual isotherms) from mixtures of benzene and* cyclo*hexane on graphite and on Spheron* 6. *Full curves, graphite: broken curves, Spheron* 6.



DISCUSSION

Examination of the Tables shows that the systems investigated can be divided into three types, representatives of which are illustrated in Figs. 5—8, where surface activity coefficients are plotted against *surface* mole-fractions. The figures also show the activity coefficients for the liquid phase plotted against mole-fractions in the *liquid* phase. This method of presentation enables a direct comparison to be made of the "escaping tendencies" of a given component from the surface layer into the liquid, and from the liquid into the vapour. The three types of behaviour are: (I) The curves of surface activity coefficient against surface mole-fraction show no point of inflexion (Fig. 5). (II) The curves do show a point of inflexion (Fig. 6). (III) The curves cross (Figs. 7 and 8).

Type I behaviour is shown by the systems which give a one-branch isotherm of concentration change and individual adsorption isotherms which show no point of inflexion. In such cases it is clear that one component of the mixture is more strongly adsorbed than the other at all concentrations. Figs. 1 and 2 each show both one- and two branched isotherms of concentration change. Fig. 4 shows examples of individual isotherms with and without points of inflexion.

Type II behaviour is shown by the majority of the systems studied. In these, the proportion of one component in the adsorbed phase is higher than in the liquid phase over part of the concentration range only, the position being reversed for the remainder of the

FIG. 5. *Surface activity coefficient curves for mixtures of benzene and* cyclo*hexane adsorbed on (A) charcoal and on (B) Spheron* 6. *Curves for the liquid phase shown broken.*

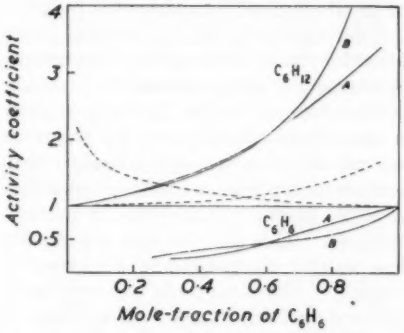


FIG. 6. *Surface activity coefficient curves for mixtures of benzene and* cyclo*hexane adsorbed on graphite.*

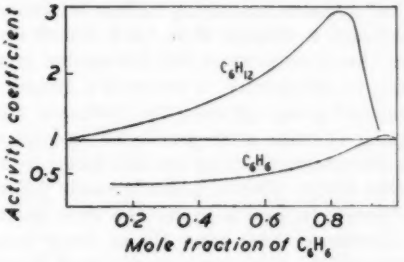


FIG. 7. *Surface activity coefficient curves for mixtures of chloroform and acetone adsorbed on charcoal. Curves for the liquid phase broken.*

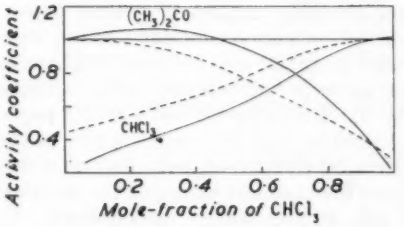
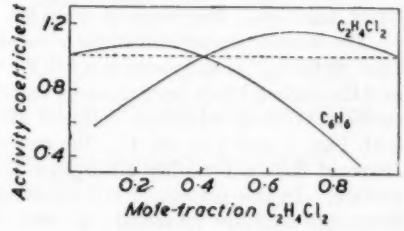


FIG. 8. *Surface activity coefficient curves for mixtures of ethylene dichloride and benzene adsorbed on charcoal. Curves for the liquid phase shown broken.*



concentration range. The pyridine–ethyl alcohol system has an isotherm of concentration change which shows only one branch, but this shows an anomalous point of inflexion and comes very close to showing a second branch. The individual isotherms do, in fact, show slight inflexions.

Type III behaviour has been found in only two systems. The chloroform–acetone system is the only one of all the systems discussed in this paper in which the activity coefficient curves for the liquid phase cross at a value below 1. This behaviour in the liquid phase is attributed to strong intermolecular attraction amounting virtually to hydrogen-bond formation (see comments in ref. 4). It seems probable that the same phenomenon occurs in the adsorbed phase.

The ethylene dichloride–benzene system shows almost ideal behaviour in the liquid phase,[7] but it is generally believed that this is due to the partial cancellation of opposing

[7] Sieg, Crutzen, and Jost, *Z. phys. Chem.*, 1951, **198**, *A*, 263.

factors.[8] In particular, there is evidence of weak association between the two substances.[9, 10] Comparison of the surface activity coefficient curves with those for the system chloroform–acetone suggests that such association may persist in the adsorbed layer.

It is possible that Type II and Type III curves are extreme forms of the same type of behaviour, for there are indications that the curves of Type II might cross if they were continued to higher mole-fractions. In this region, however, it becomes increasingly difficult to obtain results of the necessary accuracy, whether in adsorption or partial-pressure determinations. With this reservation, therefore, it is probably desirable to separate Type II and Type III behaviour. If the curves of Type II do cross, they do so only at one extreme of the concentration range. Curves of Type III, on the other hand, cross nearer the middle of the concentration range where the experimental data are much more accurate.

Two specific points may be made on the series in which close comparison is possible. The systems containing carbon tetrachloride and/or derivatives in which a methyl group replaces a chlorine atom have almost identical molecular size in each of the components, as the chlorine atom and the methyl group occupy almost the same volume. The results can be interpreted in terms of a greater affinity of the charcoal surface for the less polar methyl group (or even the hydrogen atom in the case of chloroform) than for the more polar chlorine atom (methylchloroform and chloroform are more strongly adsorbed than carbon tetrachloride), but this factor is clearly secondary in importance to that of volatility (*tert.*-butyl chloride is less strongly adsorbed than either carbon tetrachloride or methyl-chloroform, and is by far the most volatile of the three). This accords with the general experience that, other things being equal, the less volatile component of a mixture is usually the more strongly adsorbed at a charcoal surface. The same point has been made differently by Hirschler and Amon, who studied adsorption from mixed hydrocarbons on activated carbon and silica gel.[11] For a homologous series, increase in molecular weight was accompanied by increased ease of adsorption on carbon, but the reverse was found for silica gel. Increasing molecular weight in such a series brings about decreasing volatility, and we believe that the conclusion can be applied more widely in terms of the latter function. We hope to consider adsorption at oxide surfaces in a later paper.

The second comparison is the adsorption of benzene–*cyclo*hexane mixtures at the three solid surfaces. If allowance is made for the difference in surface area between the charcoal and the carbon black (as is done by considering surface mole-fractions and surface activity coefficients) their behaviour is almost identical (Fig. 5; cf. also Figs. 1 and 4 of this paper with Figs. 1 and 5 of ref. 4). We can conclude, therefore, that the porous nature of the charcoal does not modify adsorption for this system by comparison with that at a free surface. In this respect, it is interesting to compare the chemical nature of the surfaces. From the analyses (charcoal: C, 89·8; H, 1·3; ash, 3·1; O, 5·8%; carbon black: C, 95·2; H, 2·77; O, 1·09% [12]) it can be seen that the surfaces, allowance again being made for the fact that the hydrogen and oxygen are spread over a specific surface area about five times greater for the charcoal than for the carbon black, are comparable, though not identical. Both have appreciable quantities of hydrogen and oxygen chemisorbed on the surface, possibly covering a large fraction of the " carbon " surface.[13]

The sample of graphite shows very similar adsorption over most of the concentration range for this mixture, but departs from the other two adsorbents in showing slight preferential adsorption of *cyclo*hexane when it is present at low mole-fractions (Figs. 1

[8] Glasstone, *Trans. Faraday Soc.*, 1937, **33**, 158.
[9] Staveley, Hart, and Tupman, *Discuss. Faraday Soc.*, 1953, **15**, 130.
[10] Stearn and Smyth, *J. Amer. Chem. Soc.*, 1934, **56**, 1667.
[11] Hirschler and Amon, *Ind. Eng. Chem.*, 1947, **39**, 1583.
[12] Smith and Schaeffer, *Proc. 2nd Rubber Techn. Conf.*, London, 1948.
[13] Kipling, *Quart. Reviews*, 1956, **10**, 1.

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Benzene–cyclo*hexane–charcoal* ($p_1^\circ = 74{\cdot}3$; $p_2^\circ = 78{\cdot}0$).

x_1 (C_6H_6)	f_1	f_2	x_1^s	f_1^s	f_2^s	x_1 (C_6H_6)	f_1	f_2	x_1^s	f_1^s	f_2^s
0·025	2·20	1·00	0·254	0·217	1·31	0·60	1·12	1·18	0·837	0·800	2·90
0·05	1·94	1·00	0·411	0·235	1·61	0·70	1·07	1·27	0·876	0·854	3·08
0·10	1·66	1·00	0·503	0·330	1·81	0·80	1·03	1·39	0·916	0·896	3·32
0·20	1·42	1·01	0·620	0·460	2·14	0·90	1·00	1·58	0·953	0·946	3·36
0·30	1·32	1·03	0·690	0·574	2·33	0·95	1·00	1·69	0·976	0·973	3·54
0·40	1·23	1·07	0·752	0·655	2·58	0·975	1·00	1·79	—	—	—
0·50	1·17	1·12	0·795	0·733	2·74						

Monolayer values: benzene, 3·41 millimoles/g.; *cyclo*hexane, 2·64 millimoles/g.

Benzene–cyclo*hexane–Spheron* 6 ($p_1^\circ = 74{\cdot}3$; $p_2^\circ = 78{\cdot}0$).

x_1 (C_6H_6)	f_1	f_2	x_1^s	f_1^s	f_2^s	x_1 (C_6H_6)	f_1	f_2	x_1^s	f_1^s	f_2^s
0·025	2·20	1·00	0·248	0·222	1·30	0·50	1·17	1·12	0·869	0·671	4·29
0·05	1·94	1·00	0·328	0·296	1·41	0·60	1·12	1·18	0·908	0·738	5·14
0·10	1·66	1·00	0·482	0·344	1·74	0·70	1·07	1·27	0·940	0·796	6·36
0·20	1·42	1·01	0·630	0·452	2·18	0·80	1·03	1·39	0·962	0·853	7·34
0·30	1·32	1·03	0·736	0·538	2·73	0·90	1·00	1·58	0·982	0·918	8·78
0·40	1·23	1·07	0·816	0·604	3·48	0·95	1·00	1·69	0·991	0·959	9·44

Monolayer values: benzene, 0·45 millimole/g.; *cyclo*hexane, 0·40 millimole/g.

Benzene–cyclo*hexane–graphite* ($p_1^\circ = 74{\cdot}3$; $p_2^\circ = 78{\cdot}0$).

x_1 (C_6H_6)	f_1	f_2	x_1^s	f_1^s	f_2^s	x_1 (C_6H_6)	f_1	f_2	x_1^s	f_1^s	f_2^s
0·025	2·20	1·00	0·165	0·333	1·17	0·60	1·12	1·18	0·835	0·802	2·87
0·05	1·94	1·00	0·282	0·344	1·32	0·70	1·07	1·27	0·865	0·865	2·83
0·10	1·66	1·00	0·432	0·384	1·58	0·80	1·03	1·39	0·889	0·924	2·51
0·20	1·42	1·01	0·587	0·485	1·95	0·90	1·00	1·58	0·912	0·989	1·80
0·30	1·32	1·03	0·689	0·575	2·32	0·95	1·00	1·69	0·940	1·01	1·41
0·40	1·23	1·07	0·757	0·651	2·63	0·975	1·00	1·79	0·953	1·02	0·93
0·50	1·17	1·12	0·804	0·725	2·87						

Monolayer values: benzene, 0·49 millimole/g.; *cyclo*hexane, 0·41 millimole/g.

Chloroform–carbon tetrachloride–charcoal ($p_1^\circ = 160{\cdot}3$; $p_2^\circ = 91{\cdot}0$).

x_1 ($CHCl_3$)	f_1	f_2	x_1^s	f_1^s	f_2^s	x_1 ($CHCl_3$)	f_1	f_2	x_1^s	f_1^s	f_2^s
0·05	1·07	1·00	0·199	0·268	1·19	0·50	1·05	1·02	0·660	0·794	1·50
0·10	1·08	1·00	0·296	0·365	1·28	0·60	1·03	1·05	0·731	0·850	1·56
0·20	1·08	1·01	0·410	0·524	1·36	0·70	1·02	1·07	0·800	0·894	1·61
0·30	1·06	1·02	0·502	0·631	1·43	0·80	1·01	1·11	0·868	0·931	1·68
0·40	1·05	1·02	0·583	0·719	1·47	0·90	1·01	1·12	0·935	0·968	1·72

Monolayer values: chloroform, 3·85 millimoles/g.; carbon tetrachloride, 2·93 millimoles/g.

1 : 1 : 1-*Trichloroethane* (*methylchloroform*)–tert.-*butyl chloride–charcoal* ($p_1^\circ = 97{\cdot}3$; $p_2^\circ = 243{\cdot}2$).

x_1 ($CMeCl_3$)	f_1	f_2	x_1^s	f_1^s	f_2^s	x_1 ($CMeCl_3$)	f_1	f_2	x_1^s	f_1^s	f_2^s
0·10	1·25	1·00	0·265	0·472	1·22	0·60	1·05	1·02	0·817	0·770	2·24
0·20	1·13	1·01	0·464	0·487	1·50	0·70	1·03	1·03	0·876	0·826	2·51
0·30	1·11	1·01	0·584	0·572	1·70	0·80	1·02	1·04	0·917	0·891	2·51
0·40	1·09	1·01	0·671	0·647	1·85	0·90	1·01	1·05	0·958	0·952	2·50
0·50	1·07	1·01	0·748	0·714	2·01						

Monolayer values: methyl chloroform, 2·88 millimoles/g.; *tert.*-butyl chloride, 2·65 millimoles/g.

1 : 1 : 1-*Trichloroethane* (*methylchloroform*)–*carbon tetrachloride–charcoal* ($p_1^\circ = 97{\cdot}3$; $p_2^\circ = 91{\cdot}0$).

x_1 ($CMeCl_3$)	f_1	f_2	x_1^s	f_1^s	f_2^s	x_1 ($CMeCl_3$)	f_1	f_2	x_1^s	f_1^s	f_2^s
0·10	1·11	1·00	0·162	0·685	1·08	0·60	1·01	1·05	0·617	0·985	1·09
0·20	1·07	1·01	0·277	0·773	1·12	0·70	1·00	1·06	0·700	1·00	1·06
0·30	1·04	1·02	0·369	0·845	1·13	0·80	1·00	1·07	0·790	1·01	1·02
0·40	1·03	1·03	0·453	0·907	1·13	0·90	1·00	1·10	0·890	1·01	1·00
0·50	1·02	1·04	0·534	0·957	1·12						

Monolayer values: methylchloroform, 2·88 millimoles/g.; carbon tetrachloride, 2·93 millimoles/g.

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tert.-*Butyl chloride–carbon tetrachloride–charcoal* ($p_1^\circ = 243{\cdot}2$; $p_2^\circ = 91{\cdot}0$).

x_1 (Bu^{t}Cl)	f_1	f_2	x_1^s	f_1^s	f_2^s	x_1 (Bu^{t}Cl)	f_1	f_2	x_1^s	f_1^s	f_2^s
0·025	1·596	1·00	0·041	0·973	1·02	0·50	1·07	1·22	0·295	1·81	0·865
0·05	1·316	1·01	0·062	1·06	1·02	0·60	1·05	1·28	0·361	1·74	0·803
0·075	1·288	1·01	0·099	0·977	1·03	0·70	1·04	1·29	0·455	1·60	0·708
0·10	1·25	1·02	0·103	1·21	1·02	0·80	1·02	1·33	0·570	1·44	0·621
0·20	1·19	1·04	0·145	1·64	0·977	0·90	1·01	1·41	0·736	1·24	0·534
0·30	1·14	1·08	0·191	1·80	0·937	0·95	1·00	1·582	0·853	1·11	0·538
0·40	1·10	1·14	0·241	1·83	0·904						

Monolayer values: *tert.*-butyl chloride, 2·65 millimoles/g.; carbon tetrachloride, 2·93 millimoles/g.

Chloroform–acetone–charcoal ($p_1^\circ = 160{\cdot}3$; $p_2^\circ = 185{\cdot}5$).

x_1 ($CHCl_3$)	f_1	f_2	x_1^s	f_1^s	f_2^s	x_1 ($CHCl_3$)	f_1	f_2	x_1^s	f_1^s	f_2^s
0·05	0·460	0·996	0·084	0·274	1·03	0·60	0·818	0·708	0·660	0·744	0·83
0·10	0·490	0·992	0·148	0·331	1·05	0·70	0·894	0·610	0·747	0·838	0·72
0·20	0·545	0·973	0·267	0·408	1·06	0·80	0·959	0·510	0·827	0·927	0·59
0·30	0·593	0·940	0·369	0·482	1·04	0·90	0·989	0·400	0·9065	0·982	0·43
0·40	0·655	0·885	0·470	0·557	1·00	0·975	0·998	0·300	0·971	1·002	0·26
0·50	0·728	0·806	0·567	0·642	0·93						

Monolayer values: chloroform, 3·85 millimoles/g.; acetone, 4·18 millimoles/g.

Ethylene dichloride–benzene–charcoal * ($p_1^\circ = 61{\cdot}0$; $p_2^\circ = 74{\cdot}3$).

x_1 ($C_2H_4Cl_2$)	x_1^s	f_1^s	f_2^s	x_1 ($C_2H_4Cl_2$)	x_1^s	f_1^s	f_2^s	x_1 ($C_2H_4Cl_2$)	x_1^s	f_1^s	f_2^s
0·05	0·086	0·581	1·039	0·40	0·402	0·995	1·003	0·80	0·693	1·151	0·656
0·10	0·145	0·690	1·053	0·50	0·471	1·062	0·945	0·90	0·797	1·129	0·493
0·20	0·245	0·816	1·060	0·60	0·540	1·111	0·870	0·95	0·867	1·096	0·376
0·30	0·329	0·912	1·043	0·70	0·613	1·142	0·775				

* $x_1 = a_1$; $f_1 = f_2 = 1$.

Monolayer values: ethylene dichloride, 3·91 millimoles/g.; benzene, 3·41 millimoles/g.

Methyl acetate–benzene–charcoal ($p_1^\circ = 168{\cdot}4$; $p_2^\circ = 74{\cdot}3$).

x_1 (MeOAc)	f_1	f_2	x_1^s	f_1^s	f_2^s	x_1 (MeOAc)	f_1	f_2	x_1^s	f_1^s	f_2^s
0·10	1·42	1·07	0·124	1·15	1·09	0·60	1·13	1·38	0·418	1·62	0·95
0·20	1·43	1·14	0·173	1·65	1·10	0·70	1·08	1·40	0·498	1·52	0·84
0·30	1·35	1·20	0·225	1·80	1·09	0·80	1·05	1·42	0·597	1·41	0·71
0·40	1·27	1·26	0·281	1·80	1·05	0·90	1·02	1·46	0·735	1·25	0·55
0·50	1·20	1·31	0·348	1·72	1·01	0·95	1·01	1·56	0·846	1·14	0·51

Monolayer values: methyl acetate, 3·98 millimoles/g.; benzene, 3·41 millimoles/g.

Ethyl alcohol–benzene–charcoal ($p_1^\circ = 44{\cdot}7$; $p_2^\circ = 74{\cdot}3$).

x_1 (EtOH)	f_1	f_2	x_1^s	f_1^s	f_2^s	x_1 (EtOH)	f_1	f_2	x_1^s	f_1^s	f_2^s
0·025	11·4	—	0·103	2·76	—	0·60	1·26	2·05	0·263	2·87	1·11
0·05	8·28	1·04	0·138	3·00	1·15	0·70	1·12	2·43	0·301	2·61	1·04
0·10	4·97	1·08	0·178	2·79	1·19	0·80	1·05	2·85	0·379	2·22	0·919
0·20	2·87	1·20	0·203	2·82	1·21	0·90	1·02	3·66	0·534	1·72	0·785
0·30	2·10	1·33	0·219	2·88	1·19	0·95	1·01	4·18	0·701	1·37	0·699
0·40	1·69	1·51	0·230	2·95	1·18	0·975	1·00	4·48	0·840	1·17	0·700
0·50	1·45	1·74	0·241	3·01	1·15						

Monolayer values: ethyl alcohol, 5·34 millimoles/g.; benzene, 3·41 millimoles/g.

Butylamine–benzene–charcoal ($p_1^\circ = 68{\cdot}2$; $p_2^\circ = 74{\cdot}1$).

x_1 (Bu^{n}NH$_2$)	f_1	f_2	x_1^s	f_1^s	f_2^s	x_1 (Bu^{n}NH$_2$)	f_1	f_2	x_1^s	f_1^s	f_2^s
0·05	1·23	1·01	0·362	0·170	1·49	0·50	1·12	1·07	0·717	0·784	1·89
0·10	1·17	1·02	0·465	0·252	1·72	0·60	1·11	1·11	0·775	0·857	1·98
0·20	1·16	1·03	0·547	0·425	1·82	0·70	1·09	1·17	0·832	0·919	2·10
0·30	1·14	1·04	0·602	0·568	1·84	0·80	1·08	1·25	0·888	0·969	2·24
0·40	1·12	1·06	0·658	0·684	1·85	0·90	1·05	1·42	0·947	0·997	2·54

Monolayer values: *n*-butylamine, 3·39 millimoles/g.; benzene, 3·41 millimoles/g.

Pyridine–ethyl alcohol–charcoal * ($p_1^\circ = 15{\cdot}9$; $p_2^\circ = 44{\cdot}2$).

x_1 (C_5H_5N) $= a_1$	x_1^s	f_1^s	f_2^s	x_1 (C_5H_5N) $= a_1$	x_1^s	f_1^s	f_2^s	x_1 (C_5H_5N) $= a_1$	x_1^s	f_1^s	f_2^s
0·05	0·231	0·216	1·24	0·40	0·614	0·651	1·55	0·80	0·858	0·932	1·41
0·10	0·320	0·313	1·32	0·50	0·683	0·732	1·58	0·90	0·919	0·979	1·23
0·20	0·443	0·451	1·44	0·60	0·745	0·805	1·57	0·95	0·956	0·994	1·14
0·30	0·538	0·558	1·51	0·70	0·802	0·873	1·51				

* $f_1 = f_2 = 1$.

Monolayer values: pyridine, 4·10 millimoles/g.; ethyl alcohol, 5·26 millimoles/g.

XUM

and 4). In this case, the solid surface is much more nearly pure carbon (C, 97·1; H, 0·53; ash, 1·75; O, 0·61% *).

Two general points may be made. In a theoretical study, Elton [14] predicted that few cases of U-shaped isotherms of concentration change ("complete preferential adsorption") would be found, most being S-shaped. Until a more representative set of data has been collected, it is too early to say how valid this generalisation is. Nevertheless, the U-shaped isotherm is claimed to be generally observed in adsorption on active carbon from mixtures of hydrocarbons,[11, 15] and we have found it for about one-third of the mixtures used in the present study. It would be valuable to have an explanation of this phenomenon in terms of the specific forces responsible for adsorption.

Comparison of the "escaping tendencies" from the surface and from the liquid phase shows no obvious correlations, except in the two cases mentioned above in which intermolecular attractive forces are thought to be predominant in the liquid phase. For the remaining systems, absolute volatility seems to be more important than relative volatility when other factors do not intervene; this has been found previously when mixtures of paraffins are adsorbed on charcoal.[16] For most systems, however, the forces acting between the surface and the adsorbate seem to over-ride all other considerations.

Experimental

The charcoal was the steam-activated coconut-shell charcoal, washed with water as described previously.[4] The carbon black was a sample of Spheron 6 provided by Godfrey L. Cabot, Inc. The graphite was a sample of synthetic graphite of surface area 120 m.²/g., provided by Acheson Colloids Ltd.

Methods of measuring adsorption, in all cases at 20°, have already been described.[3–6] The interferometer was used for a number of the systems. Partial pressures were determined at 20° as before,[3] with the exception that taps were lubricated with a heavy "Fluorolube" fraction during work on the chlorinated compounds.

Adsorbates not previously discussed [3–6, 17] were purified as follows: Carbon tetrachloride was fractionally distilled; the sample used had n_D^{20} 1·4602, in agreement with figures quoted by Timmermans.[18] Methylchloroform was fractionally distilled; the fraction used had n_D^{20} 1·4380 (cf. 1·4379 given by Turkevich and Smyth [19]). *tert.*-Butyl chloride was washed with water, dried, and fractionally distilled; the sample used had n_D^{20} 1·3853 (cf. 1·3850 given by Hart and Simons,[20] 1·3856 by Vogel,[21] and 1·3859 by Kuschner, Crowe, and Smyth [22]). *n*-Butylamine was dried over sodium wire and fractionally distilled; the fraction used had n_D^{20} 1·4007 (cf. 1·4009 given by Vogel [23]).

Monolayer values for Spheron 6 and for graphite have been obtained from B.E.T. plots for the respective vapours. The monolayer values for benzene and *cyclo*hexane are in about the same ratio for these two adsorbents, the absolute values for graphite being slightly higher in accordance with its slightly higher surface area. These values are not, however, in accordance with the molecular areas given by Smith, Pierce, and Cordes,[24] which would require a higher adsorption of *cyclo*hexane than of benzene.

We are grateful to Godfrey L. Cabot, Inc., for the gift of Spheron 6, to Acheson Colloids Ltd. for the sample of synthetic graphite, and to Imperial Chemical Industries Ltd. for the Fluorolube lubricant.

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* We are indebted to Mr. E. R. Braithwaite, of Acheson Colloids Ltd., for this analysis.

[14] Elton, *J.*, 1952, 1955.
[15] Lloyd and Harris, *J. Phys. Chem.*, 1954, **58**, 899.
[16] Walters, *Ind. Eng. Chem.*, 1955, **47**, 2544.
[17] Kipling and Peakall, *J.*, 1956, 4828.
[18] Timmermans, "Physico-Chemical Constants of Pure Organic Compounds," Elsevier, London, 1950.
[19] Turkevich and Smyth, *J. Amer. Chem. Soc.*, 1940, **62**, 2468.
[20] Hart and Simons, *ibid.*, 1949, **71**, 345.
[21] Vogel, *J.*, 1943, 636.
[22] Kushner, Crowe, and Smyth, *J. Amer. Chem. Soc.*, 1950, **72**, 1091.
[23] Vogel, *J.*, 1948, 1825.
[24] Smith, Pierce, and Cordes, *J. Amer. Chem. Soc.*, 1950, **72**, 5595.

XUM

456. *Unstable Optical Activity in the* N-*Benzoyldiphenylamine-2-carboxylic Acid Series. Part V.**

By JEAN W. BROOKS, MARGARET M. HARRIS, and K. E. HOWLETT.

The optical stabilities of some substituted *N*-benzoyldiphenylamine-2-carboxylic acids are discussed from the viewpoint of newly determined racemisation velocity constants and of *E*, *A*, and $\Delta S^{\ddagger}$ values.

MUCH evidence [1,2,3] supports a certain sequence of optical stabilities in the series of substituted *N*-benzoyldiphenylaminecarboxylic acids (I) † which owe their optical activity to restriction of rotation about one, or perhaps two, carbon–nitrogen bonds. The velocity constants for racemisation of six such acids (the more optically stable) were measured at 20° in chloroform containing 2·5% of ethanol; [3] we now report the measurement of racemisation velocity constants for four more acids (the less optically stable) under identical conditions of solvent and concentration, so that the optical stabilities of ten acids closely related structurally can now be strictly compared at one temperature (Table 1).

TABLE 1. *Racemisation velocity constants k (min.*$^{-1}$*) for substituted* N-*benzoyldiphenylamine-2-carboxylic acids, A at* 20° *in* $CHCl_3$–2·5% EtOH *and B at* 9·9° *in* $CHCl_3$.

Acid	4	6	2′	4′	*k* (*A*)	*k* (*B*)	$t_{\frac{1}{2}}$ (*A*) (min.)	$t_{\frac{1}{2}}$ (*B*) (min.)
(I*a*)	—	Me	—	—	0·72	0·146	0·96	4·7
(I*b*)	—	Me	Me	—	0·61	—	1·1	—
(I*c*)	Br	Br	—	—	0·50	—	1·4	—
(I*d*)	Br	Br	—	Br	0·44	—	1·6	—
(I*e*)	—	Me	F	—	0·214 (0·209 *)	—	3·2	—
(I*f*)	—	Me	Cl	Me	0·166 (0·167 *)	—	4·2	—
(I*g*)	—	Me	Cl	—	0·147 *	—	4·7	—
(I*h*)	—	Me	Br	—	0·119 (0·115 *)	—	5·8	—
(I*i*)	—	Me	Cl	Cl	0·0929 *	—	7·5	—
(I*j*)	—	Me	Cl	Br	0·0862 *	—	8·0	—
(I*k*)	—	Me	—	Me	—	0·158	—	4·4

* See ref. 3.

These four acids, too unstable for resolution, were obtained optically active by crystallisation of alkaloidal salts in which a single diastereoisomer separated in approximately 100% yield (second-order asymmetric transformation). Yet another acid, *N*-benzoyl-6 : 4′-dimethyldiphenylamine-2-carboxylic acid (I*k*), could not be obtained active in this way as none of its alkaloidal salts crystallised. However, a chloroform solution of the (−)-acid was prepared by asymmetric transformation in solution (first-order) in presence of cinchonidine: the alkaloid was then removed by washing with hydrochloric acid, and the remaining chloroform solution washed, dried, and used immediately for determination of the racemisation rate. Thus a velocity constant in chloroform was obtained which could be compared with one, measured also under these enforced conditions, for *N*-benzoyl-6-methyldiphenylamine-2-carboxylic acid (I*a*). The predicted order of optical stabilities [3] has been upheld. Acid (I*a*) was not previously known as an optically active solid, although the active acid had been obtained in solution.

Racemisation velocity constants still form the most widely used criterion for comparing optical stabilities; in this work they provide a series of values which, in a roughly qualitative way, accords with predictions based on the bulk and inductive effects of groups substituted in a common skeleton. Any group added to the skeleton may change the racemisation rate in three ways: by direct electrical effects, by transmitted electrical effects, or, if it is suitably placed, sterically. It was at first somewhat surprising that

* Parts I—IV, *J.*, 1938, 1646; 1940, 264; 1955, 145, 4152.

† *Correction*: In Part IV, formula (III) (p. 4153), the R which appears in position 4 should read R′.

[1] Jamison and Turner, *J.*, 1938, 1646.

[2] *Idem*, *ibid.*, 1940, 264.

[3] Harris, Potter, and Turner, *ibid.*, 1955, 145.

there was so little difference between the velocity constants of racemisation of the 6-methyl- and the 6 : 2′-dimethyl-acid (I*a*) and (I*b*). The experimental results could be explained, to some extent at least, if addition of the second (2′) methyl group in the 6 : 2′-dimethyl-acid (I*b*) had opposing influences on the optical stability : the bulk of the methyl group increasing it and the electron-releasing power decreasing it (see ref. 3). The 6 : 4′-dimethyl-acid (I*k*) was synthesised to test this hypothesis : here the bulk effect of the methyl group is removed from the sphere of hindrance but its electrical effect remains the same as in the 6 : 2′-dimethyl-acid (I*b*). Acid (I*k*) proved to be slightly but definitely *less* stable than the 6-monomethyl-acid (I*a*) at 9·9°; therefore the remote methyl group exercises an accelerating influence on the racemisation. It should be noted in comparison that the 2′-fluoro-6-methyl-acid (I*e*) is much more stable optically than the 6 : 2′-dimethyl-acid (I*b*) in spite of the fact that the van der Waals radii of the fluorine atom and the methyl group are respectively 1·35 and 2·05 Å ;[4] in the 2′-fluoro-6-methyl-acid (I*e*) both the steric and the electrical influences of the fluorine atom appear to be decelerating relative to hydrogen.

The Arrhenius parameters E and A have been measured [1, 5, 6] for the racemisation of a variety of compounds owing their optical activity to restriction of rotation. Comparisons between the values so determined have not been entirely satisfactory [7, 8] owing, partly, to the diversity of structure in the compounds concerned and also to the different solvents and other conditions used in determining the necessary velocity constants of racemisation. As a preliminary experimental approach, racemisation velocities have been measured over a range of temperatures and E, A, and the entropies of activation $\Delta S^{\ddagger}$ (Table 2) have

TABLE 2. *Velocity constants, Arrhenius parameters, and entropy factors for racemisation.*

Acid	10^3k (sec.$^{-1}$)	Temp.	E (kcal. mole^{-1})	A (sec.$^{-1}$)	$\Delta S^{\ddagger}$ (e.u.)
Solvent : Chloroform containing 2·5% of ethanol (by volume).					
(I*a*)	1·20	20·0°	16·2	$10^{10\cdot1}$	−14·1
	0·660	13·8			
	0·327	6·9			
	0·162	0·6			
(I*c*)	0·833	20·0	19·3	$10^{12\cdot0}$	− 4·1
	0·288	10·8			
	0·0858	1·0			
	0·0817	0·6			
(I*e*)	0·663	27·4	14·9	$10^{9\cdot6}$	−20·9
	0·357	20·0			
	0·109	6·9			
(I*f*)	0·654	29·8	15·7	$10^{9\cdot1}$	−18·6
	0·277	20·0			
	0·108	10·2			
	0·0410	0·7			
(I*k*)	0·601	32·0°	16·4	$10^{9\cdot5}$	−16·9
	0·562	31·8			
	0·198	20·0			
	0·0795	10·8			
	0·0274	0·6			
Solvent : Ethanol					
(I*d*)	0·448 [a]	17·7	18·7	$10^{12\cdot3}$	− 6·9
	0·185	9·5			
	0·0603	0·65			
Solvent : Chloroform containing 6·9% of ethanol (by volume).					
(I*g*)	0·483 [b]	25·4	16·6	$10^{9\cdot7}$	−15·4
	0·308	20·6			
	0·0738	6·3			

[a] See ref. 1. [b] Potter, Thesis, London, 1953.

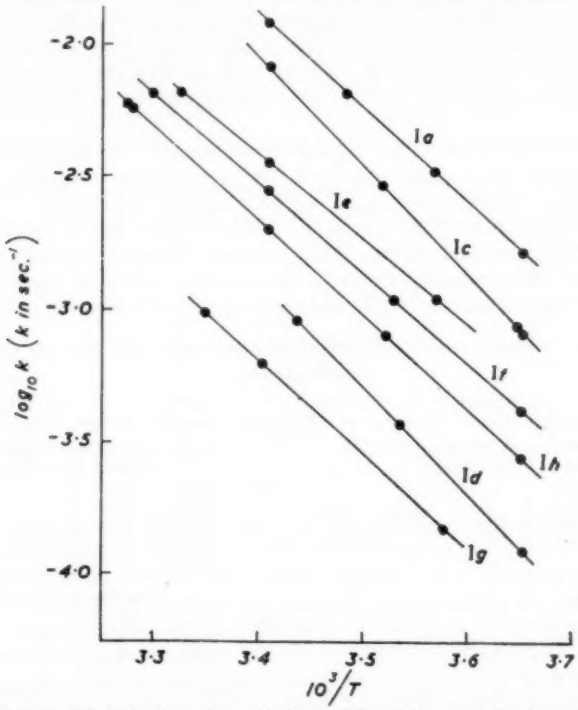
been calculated for the five substituted acids, 6-methyl-, 4 : 6-dibromo-, 2′-fluoro-6-methyl-, 2′-chloro-6 : 4′-dimethyl-, and 2′-bromo-6-methyl- (I*a*, *c*, *e*, *f* and *h*), in chloroform containing 2·5% of ethanol; two other sets of determinations for the 4 : 6 : 4′-tribromo- (I*d*) and the 2′-chloro-6-methyl-acid (I*g*), were made in different solvents.

[4] Waters, "Physical Aspects of Organic Chemistry," Routledge, London, 1950, p. 58.
[5] Kuhn and Albrecht, *Annalen*, 1927, **455**, 272; **458**, 221; Li and Adams, *J. Amer. Chem. Soc.*, 1935, **57**, 1565; Kistiakowsky and Smith, *ibid.*, 1936, **58**, 1043; Mills and Kelham, *J.*, 1937, 274; Adams and Kornblum, *J. Amer. Chem. Soc.*, 1941, **63**, 188; Rieger and Westheimer, *ibid.*, 1950, **72**, 19; Newman and Powell, *J.*, 1952, 3747; Hall, *ibid.*, 1956, 3674.
[6] Armarego and Turner, *ibid.*, 1956, 3668.
[7] Cagle and Eyring, *J. Amer. Chem. Soc.*, 1951, **73**, 5628.
[8] de la Mare, "Progress in Stereochemistry," Vol. I, Butterworths, London, 1954, p. 120.

The range of temperature employed in the determination of E is to a large extent dictated by the rapidity of racemisation at the higher temperatures and by the solubility (including the rate of dissolution) at the lower ones. Chloroform containing 2·5% of ethanol by volume has been the most generally useful solvent for the present series of acids.

The racemisation velocity constants k are calculated from $k = (1/t) \ln (\alpha_0/\alpha_t)$; as there is no asymmetric influence present, a rate constant, measured for racemisation, is twice the rate constant for inversion of configuration, the physical process occurring on the

FIG. 1. *Arrhenius plots for racemisation of substituted* N*-benzoyldiphenylamine-2-carboxylic acids.*



The plots for I*d* and I*g* have been displaced 0·7 unit lower on the $\log_{10} k$ scale.

molecular scale. In Fig. 1 $\log_{10}k$ is plotted against the reciprocal of the absolute temperature: the relation is closely linear. $\Delta S^{\ddagger}$ is calculated from the formula (see Appendix)

$$k = \kappa e(kT/h) \exp (\Delta S^{\ddagger}/R - E/RT)$$

in which E is the experimentally determined energy of activation; the transmission coefficient κ has been assumed to be unity.

It is immediately apparent that arguments based on racemisation velocity constants measured at one temperature may lead to different conclusions from those based on E values for racemisation. One can speak of either the 6-methyl- (I*a*) or the 2′-fluoro-6-methyl-acid (I*e*), for example, as the more optically stable of the two according to which criterion is used.

Scrutiny of the E, A, and $\Delta S^{\ddagger}$ values (Table 2) shows that the acids fall into two groups: (1) Those with a 6-methyl substituent have rate equations of racemisation whose

energies of activation are 14·9—16·6 kcal. mole^{-1}, A factors $10^{8\cdot6}$—$10^{10\cdot1}$ sec.$^{-1}$, and entropies of activation −14·1 to −20·9 e.u. (2) Those with a 6-bromo-substituent have the values, respectively, 18·7 and 19·3 kcal. mole^{-1}, $10^{12\cdot0}$ and $10^{12\cdot2}$, −4·1 and −6·9 e.u. The grouping of these figures is compatible with the view that among the various acids so far examined it is the resistance to relative rotation about bond (*a*) [see (I)] which is responsible for optical stability.

There are, of course, two paths by which a rotation about bond (*a*) might take place; the benzoyl group might pass the carboxylic acid group in position 2 (II) or, alternatively, it might pass the substituent in position 6 (III). If position 6 carries hydrogen only, the optical stability is very slight indeed and mutarotation is not detectable at room temperatures, even when ring A carries a chlorine atom or a methyl group in an *ortho*-position. [Interference with rotation will be less than appears in formulæ (II) and (III); for example the plane of ring A in the passing position probably lies roughly perpendicular to the plane

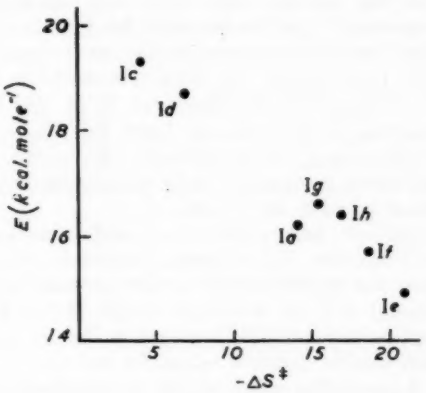
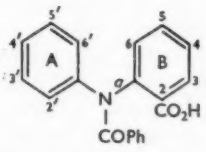
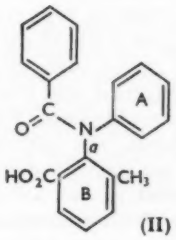


FIG. 2. *The grouping of the energies and entropies of activation.*

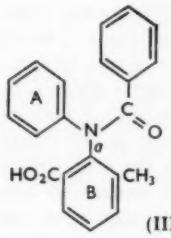
of ring B.] It is probable that structure (III) represents the most favourable passing position for the 6-methyl compounds studied, since the >C=O group would, presumably, avoid passing the similarly negative $-CO_2H$ group: Hall, Ridgwell and Turner[9] have summarised evidence which indicates that polar repulsions between two suitably placed carboxylic acid groups can exert a strongly accelerating influence on a diphenyl-type



(I; for key see Table I)



(II)



(III)

racemisation. The repulsive force envisaged in the present case would be smaller, but probably large enough to determine which of two alternative paths should be followed.

The variations of $\Delta S^{\ddagger}$ appear to make a positive contribution to the interpretation of of the optical stabilities. First, the grouping (Fig. 2) suggests a difference between the

[9] Hall, Ridgwell, and Turner, *J.*, 1954, 2498.

4 : 6-di- and the 4 : 6 : 4′-tri-bromo-acids (I*c*) and (I*d*) and the others; reference to models, and the high values of the energies of activation, support the possibility that the alternative passing position [represented by (II), but with bromine in place of methyl] might be used in these two cases. Secondly, as Cagle and Eyring [7] have pointed out in discussing the optical stability of another type of compound showing restriction of rotation, high negative values of $\Delta S^{\ddagger}$ would be expected when the transition state for racemisation is an improbable arrangement of the molecule. Foster, Cope, and Daniels,[10] studying the rearrangement of α-*cyclo*hex-1-enylallylmalononitrile to 2-allyl*cyclo*hexylidenemalononitrile by following the change in refractive index, found a fairly large negative entropy of activation and attributed it to the complicated and improbable shape which the molecule must attain for the rearrangement to take place. Models of the molecules now under discussion show that rings A and B not only must each take up favourable positions but their movements must also be synchronised for rotation about bond (*a*) to occur. Such synchronisation should be easier in the 6-methyl- (I*a*), 4 : 6-dibromo- (I*c*), and 4 : 6 : 4′-tribromo-acids (I*d*) because ring A is both unsubstituted in the *ortho*-positions and axially symmetrical; the bromo-acids (I*c*) and (I*d*) have the small negative $\Delta S^{\ddagger}$ values already noted, while the methyl-acid (I*a*) has the smallest negative value of all the 6-methyl-acids so far investigated. An *ortho*-substituent in the ring A, *i.e.*, in the 2′-fluoro-, 2′-chloro-, and 2′-bromo-6-methyl-acids (I*e*, I*f*, I*h*, and I*g*), will, both by its bulk and by its polar attractions and repulsions, lower the number of ways of attaining the transition state and will cramp movement in it. Restriction of oscillation and rotation in the activated state would be expected to be accompanied by a relatively high negative value of $\Delta S^{\ddagger}$ and such is found to be the case.

Further, within the set of acids 6-methyl- (I*a*), 2′-fluoro-6-methyl- (I*e*), 2′-chloro-6 : 4′-dimethyl- (I*f*), 2′-bromo-6-methyl- (I*h*), and 2′-chloro-6-methyl- (I*g*), there may be additional rigidity of the transition state arising from polar interactions between the carbonyl and the 6-methyl groups (III). This effect, which would also enhance the negative value of $\Delta S^{\ddagger}$, is absent in the di- and tri-bromo-acids (I*c*) and (I*d*), which have much smaller negative values for $\Delta S^{\ddagger}$.

A possibility which should be considered is that of π-hydrogen bonding between the phenyl group and the methyl group [11] which could become operative if structure (II) represented the passing position. Comparison of the $\Delta S^{\ddagger}$ values for the 6-methyl- and the 2′-fluoro-6-methyl-acid (I*a*) and (I*e*), in which ring A of (I*a*) should be the better electron donor,[12] makes this possibility seem unlikely. The values for the di- and tri-bromo-acids (I*c*) and (I*d*) are too close for valid comparison with each other, particularly as they are derived from measurements in different solvents.

In the development of arguments concerning intramolecular attractions of the hydrogen-bonding type a clear differentiation must be kept between bonds which might stabilise the (+)- and the (−)-form and those which would add rigidity to the transition complex. The former would lead to a decrease in the value of the racemisation velocity constant in the manner indicated by Jaffé, Freedman, and Doak,[13] unless they held the molecule close to the passing position thus overcoming some of the group repulsion; this effect has already been noted where formal bonds are concerned.[6] Hydrogen bonding which operates in the transition state and not (or with diminished strength) in the two interconvertible forms will become apparent in the $\Delta S^{\ddagger}$ values. A study of the effect of solvent in $k_{\text{racem.}}$, E, A, and $\Delta S^{\ddagger}$, on which preliminary experiments have already been made, should throw light on this. Chloroform, for example, might be expected to allow the greater freedom for intramolecular bonding, while ethanol would compete with the substrate and break down internal bonds in both the normal and the transition states.

[10] Foster, Cope, and Daniels, *J. Amer. Chem. Soc.*, 1947, **69**, 1893.
[11] Braude and Jackman, "Determination of Organic Structures by Physical Methods," Academic Press Inc., New York, 1955, p. 719.
[12] Tamres, *J. Amer. Chem. Soc.*, 1952, **74**, 3375.
[13] Jaffé, Freedman, and Doak, *ibid.*, 1954, **76**, 1548.

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Experimental

All measurements of rotation, α_{5461}, were made in a 2-dm. jacketed tube thermostatically controlled. " Solvent X " is chloroform containing 2·5% of ethanol by volume.

N-Benzoyl-6 : 4′-dimethyldiphenylamine-2-carboxylic Acid.—This acid was prepared by the general method [14, 1, 2] involving the Chapman rearrangement [15] of the corresponding imidate. (a) *2-Methoxycarbonyl-6-methylphenyl N-4′-methylphenylbenzimidate* was crystallised from ethanol, and had m. p. 100—101° (Found : C, 77·0; H, 6·0; N, 3·85. $C_{23}H_{21}O_3N$ requires C, 76·85; H, 5·9; N, 3·9%). (b) The imidate isomerised at 275° giving *methyl N-benzoyl-6 : 4′-dimethyldiphenylamine-2-carboxylate* which crystallised from methanol in prisms, m. p. 122° (70% yield) (Found : C, 76·3; H, 5·7; N, 3·7. $C_{23}H_{21}O_3N$ requires C, 76·85; H, 5·9; N, 3·9%). (c) *N-Benzoyl 6 : 4′-dimethyldiphenylamine-2-carboxylic acid*, crystallised from aqueous ethanol and dried (P_2O_5) in a vacuum, had m. p. 158—159° (yield 98%) (Found : C, 76·5; H, 5·53; N, 4·1. $C_{22}H_{19}O_3N$ requires C, 76·5; H, 5·56; N, 4·1).

(−)-N-Benzoyl-6 : 4′-dimethyldiphenylamine-2-carboxylic Acid in Chloroform Solution by First-order Asymmetric Transformation in Presence of Cinchonidine.—(±)-Acid (0·345 g., 0·01 mole) and cinchonidine (0·294 g., 0·01 mole) were dissolved in chloroform (25 c.c.) and set aside for 2 hr. At time $t = 0$ (min.) the solution was washed with ice-cold concentrated hydrochloric acid, then with ice–water, dried (Na_2SO_4), and filtered into a polarimeter tube previously cooled to 9·9°. At time $t = 2·80$ (min.) α was −1·61° and gradually fell to 0·0°; $k_{\text{racem.}} = 0·158$. Repetition gave an identical value for k.

Brucine (−)-N-Benzoyl-6-methyldiphenylamine-2-carboxylate.—The (±)-acid (3·31 g., 0·1 mole) and anhydrous brucine (3·94 g., 0·1 mole) were each dissolved separately in 100 c.c. of hot acetone. The mixed solutions were evaporated to 75 c.c., light petroleum (b. p. 40—60°) was added until crystallisation started, and the whole kept warm while the salt [brucine (−)-acid] crystallised (yield ≈100%). Decomposition of this salt with cold, anhydrous formic acid, followed by precipitation by dilute hydrochloric acid, gave the (−)-acid [(1) α first observed −1·94° at 0·6°, solvent X, c 0·400, $[\alpha]^{0·6°}$ −243°; (2) α first observed −5·11° at 20°, chloroform, c 1·324, $[\alpha]^{20°}$ −193°, half-life 0·96 min. at 20°].

Appendix

For a unimolecular reaction in the liquid phase $k = \kappa(\gamma^0/\gamma^\ddagger)(\boldsymbol{k}T/\boldsymbol{h})K^\ddagger$, where γ^0 and $\gamma^\ddagger$ are the activity coefficients for normal and activated reactant species respectively; $K^\ddagger = \exp(\Delta S^\ddagger/\boldsymbol{R} - \Delta H^\ddagger/\boldsymbol{R}T)$ is the expression for the modified equilibrium constant between normal and activated species.[16] If we assume that $\kappa = 1$ and that the activity coefficients are equal because the two species are so similar, and since $E = \boldsymbol{R}T^2(\mathrm{d}\log_e k/\mathrm{d}T)$ and $\mathrm{d}\log_e k/\mathrm{d}T = 1/T + \mathrm{d}\log_e K^\ddagger/\mathrm{d}T$,

$$E = \boldsymbol{R}T + \boldsymbol{R}T^2(\mathrm{d}\log_e K^\ddagger/\mathrm{d}T) = \boldsymbol{R}T + \Delta H^\ddagger - p\mathrm{d}v^\ddagger$$

where $\mathrm{d}v^\ddagger$ is the increase in volume accompanying activation. For our reactions $\mathrm{d}v^\ddagger = 0$, hence $\Delta H^\ddagger = E - \boldsymbol{R}T$ and $k = (e\boldsymbol{k}T/\boldsymbol{h})\exp(\Delta S^\ddagger/\boldsymbol{R} - E/\boldsymbol{R}T)$.

Cagle and Eyring [7] use the equation in the form $k = (\kappa\boldsymbol{k}T/\boldsymbol{h})\exp(\Delta S^\ddagger/\boldsymbol{R} - \Delta H^\ddagger/\boldsymbol{R}T)$. It is not uncommon for the experimentally determined value E to be used in place of $\Delta H^\ddagger$ in this form of the equation, an approximation which has sometimes led to confusion (see refs. 10 and 17) and which seems unnecessary in our calculations. If the approximation were used, all the $\Delta S^\ddagger$ values in Table 2 would be about two units less negative.

We thank the Department of Scientific and Industrial Research for a maintenance grant to one of us (J. W. B.).

Bedford College, University of London. [*Received, November 19th*, 1956.]

[14] Jamison and Turner, *J.*, 1937, 1954.
[15] Chapman, *ibid.*, 1929, 569.
[16] Wynne-Jones and Eyring, *J. Chem. Phys.*, 1935, **3**, 492.
[17] Daniels, " Outlines of Physical Chemistry," Wiley, New York, 1948, p. 382.

457. *The Electronic Spectrum of Formaldehyde. Part II.* Mechanisms of Dissociation of Formaldehyde and the Formaldehyde Molecular Ion.*

By J. C. D. Brand and R. I. Reed.

Predissociation in the "*A*" state of formaldehyde is discussed in terms of the value D(H–CHO) = 75·1 kcal. mole^{-1} recently obtained by electron-impact measurements.[1] In addition to the strong predissociation at 2850 Å, a second region of weak predissociation is identified at long wavelengths (~3500 Å) which strongly supports a low value for the dissociation energy of formaldehyde.

The assignment of low-lying states of formaldehyde and formyl molecular ions (CH_2O^+ and CHO^+) is considered and a set of reasonable (though not uniquely determined) adiabatic correlations is drawn for the separated states of $H + CHO^+$, $H^+ + CHO$, $H + CO^+$, etc. The results emphasise that decomposition of ions in the mass-spectrometer, in cases when the product is formed without excess of kinetic energy, almost certainly involves a radiationless transition.

The dissociation energy of formaldehyde has been discussed in many papers. Kinetic evidence [2] from the photolysis of formaldehyde [3,4] and acetaldehyde [5] supports a value for D(H–CHO) of 89—91 kcal. mole^{-1} which must represent an upper limit as in these experiments decomposition is commonly initiated at 3130 Å (91·3 kcal. mole^{-1}). The isotopic-tracer method [6] favours a much lower photochemical threshold, near 3650 Å, from which it has been argued that D(H–CHO) does not exceed 78 kcal. mole^{-1}. Electron-impact measurements with formaldehyde [1] (together with a thermochemical cycle) furnish the lowest value of all, D(H–CHO) = 75·1 $\pm$ 2·3 kcal. mole^{-1}, and this determination is the basis of the present discussion. It will be shown that a low value of D(H–CHO) offers a promising explanation of hitherto unexplained aspects of the electronic spectrum of formaldehyde.

The ionisation efficiency curves for formaldehyde have well-defined breaks, at energies greater than the appearance potential, which are assigned to excited electronic states of the molecular ions CH_2O^+ and CHO^+. The mechanism of dissociation is discussed in the following sections.

Experimental

Electron-impact measurements were made with a Metropolitan-Vickers M.S.2 spectrometer. The experimental procedure and instrumental modifications have been described previously.[1] Appearance potentials were located (within $\pm$ ~0·1 v) by the method of extrapolated voltage differences,[7] and higher breaks ($\pm$0·2—0·3 v) by the method of linear intercepts.[8] The energy distribution in the electron beam (analogue of optical slit width) restricted the resolving power of the spectrometer to *ca.* 0·3 v.

Results.—The appearance potentials and higher breaks in the ion-current curves for CH_2O^+, CHO^+, and the corresponding deuterated ions are listed in Table 1, values obtained by Price and Sugden [9] in an ionisation tube (without mass resolution) being entered for comparison. The inflection at 12·2 v (CH_2O^+) was identified at higher gas pressures only but is considered to be

* Part I, *J.*, 1956, 858.

[1] Reed, *Trans. Faraday Soc.*, 1956, **52**, 1195.
[2] Steacie, "Atomic and Free Radical Reactions," Reinhold Publ. Corp., New York, 1954, Chap. V.
[3] Calvert and Steacie, *J. Chem. Phys.*, 1951, **19**, 176.
[4] Horner, Style, and Summers, *Trans. Faraday Soc.*, 1954, **50**, 1201.
[5] Calvert, Pitts, and Thompson, *J. Amer. Chem. Soc.*, 1956, **78**, 4239.
[6] Klein and Schoen, *J. Chem. Phys.*, 1956, **24**, 1094.
[7] Warren, *Nature*, 1950, **165**, 810.
[8] McDowell and Warren, *Discuss. Faraday Soc.*, 1951, **10**, 55.
[9] Sugden and Price, *Trans. Faraday Soc.*, 1948, **44**, 116.

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real and to correspond to the 11·8 v break recorded by Price and Sugden: their inflection at 13·1 v may correspond to *A* (CHO^+), to the 13·3—13·6 v break (CH_2O^+) observed by us, or to an unresolved mixture thereof.

The particle of mass 31 in the spectrum of CH_2O is too abundant to be assigned to [$^{13}C_1$]-formaldehyde. Its appearance potential is so close to *I* (CH_2O) that it must be formed from CH_2O^+ ions by a hydrogen-transfer reaction,[10] $CH_2O^+ + H{\cdot}CHO = CH_2{\cdot}OH^+ + CHO$.

A search was also made for diffuse peaks, due to metastable ions having a low probability of dissociation or predissociation:[11] metastable D_2CO^+, HCO^+, and DCO^+ ions would occur at apparent mass-numbers (28·1, 27·1, and 27·4, respectively) which are resolved by the instrument; but none was observed.

TABLE 1.

	CH_2O^+					CO^+	
	Sudgen &					from	from
$CH_2{\cdot}OH^+$	Price [9]		CD_2O^+	CHO^+	CDO^+	CH_2O	CD_2O
10·87 ± 0·2	(10·82)	10·87 ± 0·07	10·88 ± 0·08	—	—	—	—
	11·8 ± 0·2	(12·2 ± 0·2)	—	—	—	—	—
	13·1 ± 0·2	13·6 ± 0·2	13·3 ± 0·2	13·10 ± 0·08	13·10 ± 0·12	—	—
	—	—	—	18·4 ± 0·3	18·8 ± 0·3	18·7 ± 0·2	18·8 ± 0·3

DISCUSSION

(1) *Correlation Rules.*—In the following we are concerned mainly with the decomposition of a tetratomic molecule into an atom and a triatomic molecule (*e.g.*, $CH_2O = H + CHO$), or of a triatomic molecule into an atom and a diatomic molecule. The restrictions imposed by symmetry on the permitted states of the product are governed by the symmetry elements common to the reactant, transition state, and products, and their application is subjective in that the symmetry of the transition state cannot be determined by experiment. It will be assumed that planar states of CH_2O and CH_2O^+ and non-linear states of CHO dissociate through a planar transition state (C_s), (I) or (II); and that linear states of CHO or CHO^+ dissociate through a linear transition state ($C_{\infty v}$). The form of

(I)

(II)

(III)

the correlation rules is the same for ions and uncharged molecules. Because the excitation energy of H and H^+ is large we need consider only those rules [12] which relate to S_g atomic states (Table 2 and 3). However, there is the further possibility [2] of molecular decomposition of the type, $H_2CO = H_2 + CO$, presumably by way of a C_{2v} transition state (III),

TABLE 2. *Correlation rules for the reaction* $H_2CO = H + HCO$. In the decomposition of a pyramidal (C_s) state of formaldehyde the transition state (C_1) has no symmetry element and all correlations are permitted subject to the multiplicity rules.

Species B_2 and B_1 are defined as, respectively, *s* and *a* to the molecular plane, σ_{yz}, of a C_{2v} formaldehyde. This is the reverse of the convention adopted in Part I. The resolution of the species of C_{2v} into those of C_s is contained in the first two columns of the Table.

Reactant	Transition state	Atom + triatomic molecule	
C_{2v}	C_s	$C_{\infty v}$	C_s
A_1, B_2	A'	$S_g + \Sigma^+$, π, Δ . . .	or A'
A_2, B_1	A''	$S_g + \Sigma^-$, π, Δ . . .	or A''

and the rules for this case are given in Table 4. In addition to the permitted orbital correlations the same multiplicity rules hold as for diatomic molecules.[13]

[10] Norton, Nat. Bur. Stand. Circ. 522, p. 201.
[11] Hipple, Fox, and Condon, *Phys. Rev.*, 1946, **69**, 347.
[12] Shuler, *J. Chem. Phys.*, 1953, **21**, 624.
[13] Herzberg, "Spectra of Diatomic Molecules," Van Nostrand, New York, 1950, p. 319.

TABLE 3. *Correlation rules for the dissociation of linear states of* HCO^+. Atomic states other than S_g are not considered here. The correlation rules for the dissociation of non-linear states can be read from the second and the final column of Table 2.

Products →	$C_{\infty v}$	Σ^+	Σ^-	π	Δ	..
Atom		Reactant				
S_g		Σ^+	Σ^-	π	Δ	..

TABLE 4. *Correlation rules for molecular dissociation,* $H_2CO = H_2 + CO$.

Products →	H_2	Σ_g^+	Σ_u^+	Σ_g^-	Σ_u^-	$\pi_g, \Delta_u \ldots, \pi_u, \Delta_g \ldots$	
CO		Reactant (C_{2v})					
Σ^+	A_1	B_2	B_1	A_2	$A_2 + B_2$	$A_1 + B_1$
Σ^-	A_2	B_1	B_2	A_1	$A_1 + B_1$	$A_2 + B_2$
π	$B_1 + B_2$	$A_1 + A_2$	$A_1 + A_2$	$B_1 + B_2$	$A_1 + A_2 + B_1 + B_2$	
Δ	$A_1 + A_2$	$B_1 + B_2$	$B_1 + B_2$	$A_1 + A_2$	"	
...	...	...	...	...	...	

In constructing correlation curves for the electronic states of reactants and products it will be recalled that the crossing of states of the same symmetry species is not forbidden for more-than-diatomic molecules.[14] Subject to the Franck–Condon principle, radiationless transitions between electronic states of the same symmetry (equivalent to homogeneous perturbations of the states of diatomic molecules) may have high probability in the critical region of a crossing, and radiationless transitions between states of different symmetry may be permitted when vibrational-electronic interaction is taken into account.[15] The rules in Table 2—4 apply therefore to vibronic states as well as to purely electronic states. Symmetry considerations place relatively few restrictions on the permitted states of the products of an adiabatic decomposition.

In Table 5 are listed the heats of formation of the separated states of H + HCO, H^+ + HCO, H + CO^+, etc., which require consideration in drawing up sections of the electronic term manifold of H_2CO, H_2CO^+, and HCO^+. References to the thermochemical and spectroscopic sources are given in the Appendix.

TABLE 5.

Reactant	Separated states of product	Multiplicity	Energy relative to CH_2O ($^1A_1$) (kcal. mole^{-1})	(ev)
HCO^+	$H^+(^1S_g) + CO(^1\Sigma^+)$	1	367	15·91
	$H(^2S_g) + CO^+(^2\Sigma^+)$	1, 3	376	16·32
	$H(^2S_g) + CO^+(^2\pi_i)$	1, 3	435	18·89
H_2CO	$H_2(^1\Sigma_g^+) + CO(^1\Sigma^+)$	1	1·3	0·05
	$H(^2S_g) + HCO(^2A'')$	1, 3	75·1	3·26
	$H(^2S_g) + HCO(^2\Sigma^+)$	1, 3	99·4	4·31
	$2H(^2S_g) + CO(^1\Sigma^+)$	1, 3	105	4·58
H_2CO^+	$H(^2S_g) + HCO^+(^1\Sigma^+)$	2	303	13·13
	$H_2(^1\Sigma_g^+) + CO^+(^2\Sigma^+)$	2	324	14·06
	$H_2^+(^2\Sigma_g^+) + CO(^1\Sigma^+)$	2	357	15·48
	$H^+(^1S_g) + HCO(^2A'')$	2	388	16·86
	$H^+(^1S_g) + HCO(^2\Sigma^+)$	2	413	17·91
	$H^+(^1S_g) + H(^2S_g) + CO(^1\Sigma^+)$	2	418	18·17
	$2H(^2S_g) + CO(^2\Sigma^+)$	2, 2, 4	428	18·58

(2) *Predissociation of Formaldehyde.*—According to the electron-impact measurement,[1] D(H–CHO) = 75·1 kcal., the ground state of CHO is lower in energy than the first excited

[14] Teller, *J. Phys. Chem.*, 1937, **41**, 109.
[15] Sponer and Teller, *Rev. Mod. Phys.*, 1941, **13**, 75.

singlet state of formaldehyde (28,198 cm.$^{-1}$ = 80·6 kcal. mole^{-1}) (Part I). The possibility exists, therefore, of predissociation covering the whole band system which, in regard to absorption from the vibrationless ground state, stretches from 3550 to below 2500 Å; this is consistent with the photolysis studies,[6] but in the present section we shall be concerned with purely spectral evidence. It is well known that the absorption is diffuse at wavelengths less than ~2850 Å [16, 17] but at the long-wavelength end of the spectrum the rotational line-width (*ca.* 0·1 cm.$^{-1}$) [19] does not exceed the Döppler broadening and the probability of dissociation must be quite small.

The evidence for predissociation near the zero-point level of the excited state is twofold: the impurity of the electronic wave function and the inactivity in emission of low-lying vibrational levels. Fig. 1 represents the levels of the zeroth and first quanta of the

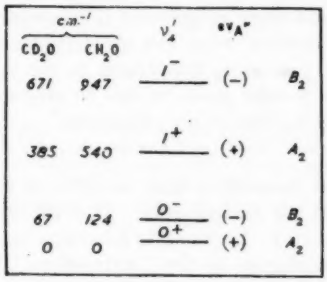

FIG. 1. *Low-lying A'' vibronic states of excited formaldehyde. In addition to the C_s symmetry of the nuclei, the potential field has C_2 symmetry on account of the inversion doubling and the +, − classification defines the character of the wavefunctions under the operations of the groups C_2. Equivalent species of a C_{2v} formaldehyde are given on the extreme right.*

wagging vibration, $\nu_4(\omega CH_2)a'$, of the $^{c1}A''$ (C_s) excited state, each level being split into inversion doublets by the non-planar geometry of the nuclei. The levels active in fluorescence are those in Fig. 1, plus combinations with one or two quanta of $\nu_3(\nu CO)a'$; the number of bands recorded (Part I) from each of the emitting levels is given in Table 6.

TABLE 6.

		[$^2H_1$]Formaldehyde		[$^2H_2$]Formaldehyde	
ν_4	ν_3	Height (cm.$^{-1}$)	No. of bands in emission	Height (cm.$^{-1}$)	No. of bands in emission
0^+	0	0	6	0	18
0^-	0	124	7	67	15
1^+	0	540	—	385	5
1^-	0	947	—	671	2
0^+	1	1171	3	1178	2
0^-	1	1308	1	1243	2
1^+	1	2150	—	1559	1
0^+	2	2323	1	2336	1

In the present paper the notation for the fundamental vibrational modes follows the recommendation of the recent Report (*J. Chem. Phys.*, 1955, **23**, 1997). The symbols for the totally symmetrical modes of excited ($^cA''$) formaldehyde are summarised below.

		Frequency (cm.$^{-1}$)				Frequency (cm.$^{-1}$)	
This paper	Part I	CH_2O	CD_2O	This paper	Part I	CH_2O	CD_2O
$\nu_1(\nu CH)a'$	ν(CH)	2875	2078	$\nu_3(\nu CO)a'$	ν(CO)	1182	1176
$\nu_2(\delta CH_2)a'$	$\delta(CH_2)$	1322	989	$\nu_4(\omega CH_2)a'$	$\gamma(CH_2)$	682	494

It will be seen that no transitions are observed from the levels $\nu_4 = 1^+$, 1^- of [$^1H_2$]formaldehyde * although they are present in approximately the expected abundance in the

* The existence of the 1^+ level has been queried because of its inactivity in fluorescence: [19a] this objection lacks appreciation of the fact that at least five transitions are recorded from this level in the spectrum of [$^2H_2$]formaldehyde.

[16] Schou, *J. Chim. phys.*, 1928, **25**, 655; 1929, **26**, 1.
[17] Herzberg, *Trans. Faraday Soc.*, 1931, **27**, 378.
[18] Dieke and Kistiakowsky, *Phys. Rev.*, 1934, **45**, 4.
[19] Robinson, (*a*) *Canad. J. Phys.*, 1956, **34**, 699; (*b*) *J. Chem. Phys.*, 1954, **22**, 1384.

spectrum of [$^2H_2$]formaldehyde. The possibility that the excitation fails to populate the 1^+ and 1^- levels seems remote. Excitation has usually been in an electric discharge but the conditions [19b, 20] vary considerably from those in Part I and in no case has emission been reported from the 1^+ and 1^- vibrational states; moreover, if the excitation were responsible, it should be selective for both [$^1H_2$]- and [$^2H_2$]-formaldehyde. We conclude that the " missing " levels indicate a predissociation which sets as an upper limit D(H–CHO) $\leqslant$ 28,736 cm.$^{-1}$ (82·3 kcal. mole^{-1}).

The second relevant observation is that the vibrationless ground state of formaldehyde combines in absorption with the $\nu_4(\omega CH_2)a' = 0^+$, 1^+ levels of the $^eA''$ state and with combinations of them with $\nu_2(\delta CH_2)a'$ and $\nu_3(\nu CO)a'$ (Part I). The transitions are of type A, and of very low intensity compared with the main absorption bands (which are of type B), but they are present in the spectra of [$^1H_2$]-, [$^2H_1$]-, and [$^2H_2$]-formaldehyde and their assignment is non-equivocal. These type A bands are allowed by the overall selection rules but are forbidden by the asymmetric top rules: vibronically, they are $A_1 \longleftrightarrow A_2$ transitions in the C_{2v} notation (Fig. 1). The breakdown of the asymmetric top rules must be due to the approximation implicit in the factorisation of the overall gyrovibronic wavefunction,

$$\psi_{evr} = \psi_e\psi_v\psi_r$$

of the excited state, and this in turn indicates a perturbation operating on the ψ_e function of the excited state. Specifically the observation of the type A transitions means that the $^eA''$ upper state has some $^eA'$ character, the presence of the type A bands being then analogous to the " extra-lines " in diatomic molecule spectra. It is natural to assume that the perturbing $^eA'$ state is associated with the predissociation of the $^eA''$ state discussed above, and therefore that the predissociation involves an $A'' \longrightarrow A'$ radiationless transition to a dissociative A' state. The radiationless transition must have a very low probability, for it is sufficient to interrupt emission only from excited vibrational states of ν_4: and, conversely, the probability must increase with increasing amplitude of ν_4. As the turning points of the vibration are symmetrically placed on each side of the inversion plane of the $^eA''$ state we conclude that the perturbing $^eA'$ state is strongly pyramidal, and the smaller efficiency of predissociation from $\nu_4 = 1$ levels of [$^2H_2$]formaldehyde can then be understood in terms of the smaller vibrational amplitude.

The lowest known electronic state of CHO is $^2A''$, provisionally regarded as the ground state.[21] This $^2A''$ state cannot be correlated with the $^1A_1$ ground state of formaldehyde (Table 2), or with a stable excited state of formaldehyde because none is available; it must correlate with a dissociative state. Conversely, the unstable $^eA'$ state of formaldehyde must correlate with the $^2A''$ state of formyl unless there exists another, very low-lying, state of formyl at present unknown. The adiabatic dissociation

$$CH_2O^* (^eA') \longrightarrow H (^2S_g) + CHO (^2A'') \quad . \quad . \quad . \quad . \quad . \quad (1)$$

is permitted (Table 2) because the reactant and the product have no common element of symmetry. In terms of one-electron wave functions, the lowest $^eA'$ state of formaldehyde results from a π–π' promotion (expected to lead to a strongly pyramidal state [22])

$$KK\ (\sigma_1, a_1)^2(\sigma_2, a_1)^2(\sigma_3, a_1)^2(\sigma_4, b_2)^2(\pi, b_1)^2(n, b_2)^2 : {}^1A_1 \longrightarrow$$
$$KK\ (\sigma_1, a')^2(\sigma_2, a')^2(\sigma_3, a')^2(\sigma_4, a'')^2(n_1, a')(n_2, a'')^2(n_3, a') : {}^{1,3}A' \quad . \quad (2)$$

where n_1, n_2 . . . signify mainly non-bonding orbitals.

Configuration interaction blurs the outline of the representation in (2), but we conclude that the upper state is unstable and that it " crosses " the surfaces of the $^eA''$ state (n–π')

[20] Schuler, *Spectrochim. Acta*, 1950, **4**, 85.
[21] Herzberg and Ramsay, *Proc. Roy. Soc.*, 1955, *A*, **233**, 34.
[22] Walsh, *J.*, 1953, 2288, 2306.

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in the region of the electronic origin.* A consequence of this explanation is that the banded spectrum of formaldehyde should be superimposed on a weak continuum. The dissociation of the $^{e}A'$ state according to (1) may explain why the analogue of an $N \longrightarrow V$ transition of formaldehyde has not been satisfactorily identified.

Beyond 2850 Å formaldehyde shows a second, much stronger predissociation,[16,17] the onset being somewhat above the energy of the first excited, $^{2}\Sigma^{+}$, state [21] of CHO. The decomposition

$$H_2CO\ (^1A_1) \ldots\ldots H\ (^2S_g) + HCO\ (^2\Sigma^+) \quad . \quad . \quad . \quad . \quad . \quad (3)$$

being permitted, it is natural to correlate the $^{2}\Sigma^{+}$ state with a dissociation limit of the A_1 ground state of formaldehyde. The second predissociation of the A'' state therefore

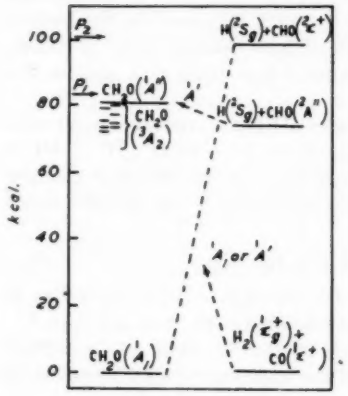


FIG. 2. *Arrows on the left mark the two predissociations in the* $^{1}A''$ *excited state. The short leading lines mark known vibrational levels of a low-lying state,* $^{3}A_2$ *or* $^{3}A''$ *(Cohen and Reid,* J. Chem. Phys., 1956, **24**, 85), *of* $[^1H_2]$-^{19a} *and* $[^3H_2]$-*formaldehyde: the position of the zero-point level of this state is uncertain.*

FIG. 3. *The energy scale (ordinate) is relative to the ground state of* CH_2O.

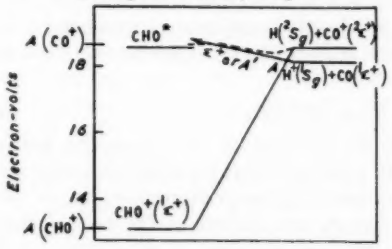
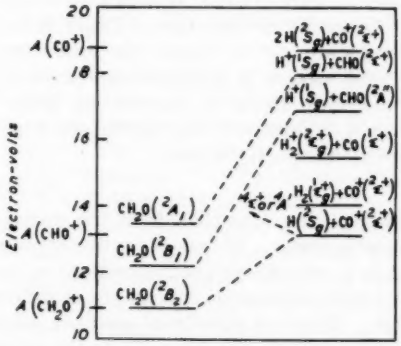


FIG. 4. *Cf. legend to Fig. 3.*



involves an $^{e}A'' \longrightarrow {}^{e}A_1$ radiationless transition to levels of the ground state of formaldehyde above the dissociation limit. The interpretation of both predissociations is summarised in Fig. 2.

(3) *States of* CHO^+.—The ground state of CHO^+ is lower in energy than that of the dissociation products ($H^+ + CO$ and $H + CO^+$) by at least 5 ev, in agreement with expectation for the stable electron configuration,

$$KK\sigma_1^2\sigma_2^2\sigma_3^2\pi_1^4\ :\ ^1\Sigma^+ \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (3)$$

In Fig. 3 the dissociation of the ground state is correlated adiabatically with the separated states $H\ (^2S_g) + CO^+\ (^2\Sigma^+)$ on the ground that the electron configuration,

* The mixing potential must have *a''* symmetry. It may be encompassed by a rotation about the axis of least inertia, for it is known from high-resolution measurements that the 1^- level of $[^1H_2]$formaldehyde has an abnormal dependence of the rotational energy levels on K.[18] But the rotational perturbation may have a different explanation (Part I and ref. [19a]).

$KK\sigma_1^2\sigma_2^2\pi_1^4\sigma_3 : {}^2\Sigma^+$ of CO^+ is precisely that expected to form a strong bond with a hydrogen atom.[23] This correlation is permitted for the dissociation of a linear triatomic molecule through a linear transition state (Table 3). The excited states of CHO^+ will involve the promotion of a π_1 electron (eqn. 3) to an antibonding π_2^1 or σ_4^1 orbital, probably accompanied by reorganisation to a non-linear configuration.[22] According to the electron-impact data the first stable excited state is reached by a vertical excitation of 5·3—5·6 v.

On the assumptions underlying Fig. 3 the separated states $H^+ ({}^1S_g) + CO ({}^1\Sigma^+)$ have to be correlated with an unstable $^1\Sigma^+$ or $^1A'$ excited state of CHO^+ : interaction at the crossing-point A (Fig. 3) is not expected to be unduly great because the electron configurations differ considerably. The production of CO^+ ions, without excess of kinetic energy,[1] may be explained by direct predissociation from the stable excited state, or by induced predissociation through the unstable excited state (*i.e.*, the path indicated by the broken line in Fig. 3). In electron-impact studies, production of ions *without excess of kinetic energy* is a powerful argument in support of a radiationless transition as a step in the mechanism of decomposition.

(4) *States of* CH_2O^+.—The ground and first excited states of CH_2O^+ are stable to possible forms of dissociation, for the states of the separated products, $H + HCO^+$, $H^+ + HCO$, $H_2 + CO^+$, and $H_2^+ + CO$, all lie at considerably greater energy. From the single-electron configurations[9] it would be predicted that the low-lying states of H_2CO^+ are doublet states with the nuclear configuration C_{2v}. The ground state :

$$KK(\sigma_1, a_1)^2(\sigma_2, a_1)^2(\sigma_3, a_1)^2(\sigma_4, b_2)^2(\pi, b_1)^2(n, b_2) : {}^2B_2 \quad . \quad . \quad . \quad . \quad (4)$$

is expected to correlate with the lowest state of the products, $H ({}^2S_g) + HCO^+ ({}^1\Sigma^+)$ (Fig. 4) which, according to the rules in Table 2, may be formed adiabatically from a $^2B_2$ or $^2A_1$ state of CH_2O^+. On this basis the dissociation energy of the $^2B_2$ state (4) is 2·23 ev (Table 1), the low value being explained by the fact that the approach of a hydrogen atom to the $^1\Sigma^+$ state of CHO^+ throws a bonding pair of electrons out of the CO bond region.

The second excited state of CH_2O^+ is higher in energy than the dissociation limit of the ground state and to explain the production of HCO^+ ions without excess kinetic energy we must assume a radiationless transition from the first excited state to levels of the ground state above its dissociation limit. If the single-configuration molecular-orbital theory is qualitatively dependable, the first excited state of H_2CO^+ is reached by a $\pi \longrightarrow n$ promotion (eqn. 4) yielding :

$$\ldots\ldots\ldots (\sigma_4, b_2)^2(\pi, b_1)(n, b_2)^2 : {}^2B_1 \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (5)$$

A radiationless transition from the state (4) to (5) is forbidden as a transition between electronic states. It may occur by coupling with rotation about the figure axis (this would lead to a very feeble predissociation) or as a transition between vibronic states in which non-totally symmetric vibrations of different species are excited in the two electronic states. This type of induced predissociation has not been observed in polyatomic spectra. It is forbidden by the Franck–Condon principle but may attain appreciable probability in the region of a dissociation limit where the potentials are far from harmonic.

Appendix

Standard enthalpies of formation, ΔH_f°, *in the gaseous state at* 1 *atm. and* 25° (kcal. mole^{-1}) : Hydrogen atoms,[24a] 52·1; carbon monoxide,[24a] −26·42; formyl radical,[1] −4·7; formaldehyde,[24a] −27·7.

Ionisation potentials (electron-volts) : hydrogen atoms,[24b] 13·595; carbon monoxide, 14·01; formyl radical,[1] 9·87; formaldehyde,[1] 10·87; hydrogen,[25] 15·43.

Excitation energies (electron-volts) : CHO ($^2\Sigma^+$),[21] 1·05; CH_2O ($^1A''$), 3·50 (Part I); CO and CO^+, ref.[13], Table 39.

The University, Glasgow, W.2. [*Received, December* 14*th*, 1956.]

[23] Linnett, *J.*, 1956, 275.
[24] Nat. Bur. Stand., (*a*) Circ. 500, 1949; (*b*) Circ. 467, 1948.
[25] Beutler and Junger, *Z. Physik*, 1936, **100**, 80.

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458. 1 : 1 : 1-*Trifluoro*-2 : 3-*dione Dioximes and Related Compounds.*

By R. Belcher, A. Sykes, and J. C. Tatlow.

The direct bromination of ethyl trifluoromethyl ketone in sulphuric acid gave 3-bromo-1 : 1 : 1-trifluorobutan-2-one. With bromine in sodium acetate–acetic acid each of these ketones gave 3 : 3-dibromo-1 : 1 : 1-trifluorobutan-2-one. This was converted by hydroxylamine into 1 : 1 : 1-trifluorobutane-2 : 3-dione dioxime, which showed unusual properties when treated with ammoniacal nickel solutions. Hydrolysis of the dioxime, or treatment of ethyl trifluoromethyl ketone with selenium dioxide, gave the diketone, isolated as the quinoxaline derivative. 3 : 3-Dibromo-1 : 1 : 1-trifluoroacetone and hydroxylamine gave the dioxime of 3 : 3 : 3-trifluoropyruvaldehyde; with semicarbazide, either the analogous disemicarbazone, or the semicarbazone of the parent ketone, was formed according to the conditions.

Certain 1 : 2-dioximes are well known as analytical reagents for the determination of nickel and some other metal ions.[1] In connection with our studies of fluorine-containing compounds as possible analytical reagents, an investigation of dioximes possessing trifluoromethyl substituents was undertaken. No success was achieved in attempts to make a hydroxyimino-derivative from ethyl trifluoromethyl ketone, and so the desired dioximes were made by extensions of the work of McBee and Burton [2] who brominated 1 : 1 : 1-trifluoroacetone with bromine in concentrated sulphuric acid to give 3 : 3-dibromo-1 : 1 : 1-trifluoroacetone which, with semicarbazide, gave the disemicarbazone of 3 : 3 : 3-trifluoropyruvaldehyde, with loss of bromine. We found that, in the cold, the dibromo-ketone gave a monosemicarbazone in the usual way. The disemicarbazone of the keto-aldehyde was formed only at elevated temperatures. The dioxime was prepared similarly.

Ethyl trifluoromethyl ketone with bromine (0·5 mol.) in concentrated sulphuric acid gave 3-bromo-1 : 1 : 1-trifluorobutan-2-one. In this reaction only half-molar quantities of bromine are necessary,[2] but 1 mol. of bromine under these conditions also gave only the monobromo-compound and no dibromide. However, the latter ketone, 3 : 3-dibromo-1 : 1 : 1-trifluorobutan-2-one, was prepared by direct bromination of ethyl trifluoromethyl ketone or of 3-bromo-1 : 1 : 1-trifluorobutan-2-one in sodium acetate–acetic acid.

α-Nitrato-ketones have been made [3] by the action of silver nitrate on solutions of α-bromo-ketones in dry acetonitrile, and aryl α-diketones have been prepared from them [4] by the action of a base. 3-Bromo-1 : 1 : 1-trifluorobutan-2-one reacted with silver nitrate in dry acetonitrile to give silver bromide in 92% yield, but the attempted isolation of the α-nitrato-ketone, and subsequent conversion into an α-diketone, failed. When treated with semicarbazide in the cold, 3-bromo-1 : 1 : 1-trifluorobutan-2-one gave a monosemicarbazone.

Treatment of 3 : 3-dibromo-1 : 1 : 1-trifluorobutan-2-one with hydroxylamine hydrochloride in sodium acetate solution gave 1 : 1 : 1-trifluorobutane-2 : 3-dione dioxime as a crude mixture, from which one form was isolated as a crystalline solid, m. p. 89°. This compound reacted with nickel ions in ammoniacal solution to give a drab green precipitate, which was virtually insoluble in carbon tetrachloride, chloroform, etc. Analysis of this precipitate gave poor results but indicated that it was a 1 : 1 compound of the dioxime with nickel. However, the oily residues remaining after the separation of this crystalline

[1] (*a*) Tschugaeff, *Z. anorg. Chem.*, 1905, **46**, 144; (*b*) Diehl, "The Applications of the Dioximes to Analytical Chemistry," G. F. Smith Chemical Co., Colombus (Ohio), 1940.
[2] McBee and Burton, *J. Amer. Chem. Soc.*, 1952, **74**, 3902.
[3] Ferris, McLean, Marks, and Emmons, *ibid.*, 1953, **75**, 4078.
[4] Emmons and Freeman, *ibid.*, 1955, **77**, 4415.

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dioxime reacted differently with nickel ions in ammonia solution, giving, as well as the green form, a bright red precipitate which could be extracted by chloroform and by carbon tetrachloride. Accordingly, the preparation of the dioxime was repeated, the crude product was treated with ammoniacal nickel sulphate solution and the red precipitate, which was formed simultaneously with the drab green one, was extracted into chloroform. Analysis of the red solid obtained from the chloroform extracts confirmed that this compound contained 2 molecules of dioxime and 1 atom of nickel and was thus analogous to the complexes formed by dimethylglyoxime and similar reagents.[1]

In an attempt to liberate the parent dioxime from the red nickel derivative, the complex was decomposed with hydrochloric acid. However, the dioxime which was isolated had m. p. and mixed m. p. 89° and reacted with an ammoniacal nickel solution to give only the drab green precipitate. The dioxime preparation was again repeated and a sample of the crude product treated with an ammoniacal nickel solution to demonstrate the formation of the two compounds. When the remainder of the crude dioxime was treated with hydrochloric acid, recovered by ether-extraction, and then treated with an ammoniacal nickel solution, only the green precipitate was formed. Thus, the form of the dioxime giving the red complex was unstable to acid, being converted into the crystalline form, m. p. 89°. Accordingly, the dioxime preparation was carried out in sodium carbonate solution, but it was possible to isolate only the same solid, m. p. 89°, although treatment of a sample of the crude product with nickel ions, in the usual way, gave both nickel compounds, thus showing that both forms of the dioxime were again present. As an alternative, an attempt was made to convert the dioxime, m. p. 89°, into the form which gave the red complex by digestion with 2N-ammonia (pH 12), but the organic compound was degraded and fluoride ion was found in the aqueous solution. Both the crystalline dioxime and the oily residues reacted with palladium ions in aqueous solution. The former gave a cream-coloured precipitate, insoluble in chloroform and in carbon tetrachloride, while the latter gave a golden-yellow one, soluble in these solvents. Though analyses of them were rather unsatisfactory, these compounds resembled those formed by nickel.

From aromatic 1 : 2-dioximes, such as benzil dioxime, three different stereochemical forms have been isolated and shown [5, 6] to react differently with nickel ions. The α(*anti*)-form gave a red (2 : 1) complex, the β(*syn*)-form gave no precipitate, and the γ(*amphi*)-form gave a yellow (1 : 1) compound. The green nickel derivative of the crystalline dioxime isolated in the present work resembles those from γ-dioximes.[5, 1b] In the formation of the compound between one molecule of dioxime and one atom of nickel the hydrogen atoms of both oxime groups are replaced by the metal, so that the resulting product is salt-like rather than a chelate compound, and this will account for its insolubility in organic solvents. So far as we can ascertain, known examples of aliphatic 1 : 2-dioximes react with nickel ions to give only the red (2 : 1) precipitates, although a transient yellow compound is first formed when a solution of dimethylglyoxime in acetone is added to a dilute and very weakly acidic solution of a nickel salt.[1b] The evidence therefore indicates that the dioxime, m. p. 89°, described here is unique, at least in the aliphatic series, in being a stable γ(*amphi*)-form. Since R = Me and R′ = CF_3, two such forms are possible, so that the compound might be a mixture. Since the crude dioxime also yields the red (2 : 1) nickel complex, the *anti*-form of the dioxime is presumably also present, though it appears to be less stable.

Hydrolysis of the crystalline dioxime with hydrochloric acid gave the parent diketone, which could not be isolated in a pure condition. The crude product was characterised, however, since with *o*-phenylenediamine, 2-methyl-3-trifluoromethylquinoxaline was formed. The oxidation of ethyl trifluoromethyl ketone with selenium dioxide was also studied. In aqueous solution, the reaction was slow, only half complete after 15 hr., as

[5] Atack, *J.*, 1913, **103**, 1317.
[6] Tschugaeff, *Ber.*, 1908, **41**, 1678.

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indicated by the recovery of selenium; about 40 hr. was required for the completion of the oxidation. The product was heterogeneous and contained selenium, probably as organic complexes, which have been obtained from other oxidations with selenium dioxide. Attempts to prepare a more tractable product by carrying out the reaction in ethyl alcohol or dioxan were not successful. The crude α-diketone gave 1 : 1 : 1-trifluorobutane-2 : 3-dione dioxime (m. p. 89°) when treated with hydroxylamine hydrochloride in sodium acetate solution, whilst treatment with *o*-phenylenediamine gave 2-methyl-3-trifluoromethylquinoxaline. It is probable that isolation of this diketone from these experiments was complicated by hydrate formation.

Experimental

Ethyl Trifluoromethyl Ketone.—Trifluoroacetic acid was treated with ethylmagnesium iodide by the method of Sykes, Tatlow, and Thomas [7] to give the desired ketone (52%), b. p. 45—45·5°.

Preparation of 3-Bromo-1 : 1 : 1-trifluorobutan-2-one.—Ethyl trifluoromethyl ketone (39·2 g.) and concentrated sulphuric acid (130 c.c.) were stirred at 15—20° whilst bromine (25·0 g.) was added slowly. The stirring was continued at 15—20° for 6 hr. and then at 60—70° for ½ hr., sulphur dioxide being collected in a trap cooled by solid carbon dioxide–ethyl alcohol. The mixture was cooled and the two layers were separated. Volatile components were distilled from the lower (acid) layer through a 1′ column packed with 4 mm. single-turn Fenske glass helices. The distillate was added to the upper layer, which was distilled (1′ column) to give a fraction (48·5 g.), b. p. 92·5—93·5°. This was shaken with silver powder and redistilled, to give 3-bromo-1 : 1 : 1-trifluorobutan-2-one (47·3 g.), b. p. 92·5—93·5°, n_D^{20} 1·3792 (Found: C, 23·2; H, 2·0. Calc. for $C_4H_4OBrF_3$: C, 23·4; H, 2·0%). This compound had a strong infrared absorption band at 1757 cm.$^{-1}$. It has been prepared also by Rausch, Lovelace, and Coleman.[10]

In a similar experiment, ethyl trifluoromethyl ketone (20·0 g.) was stirred with concentrated sulphuric acid (100 c.c.) at 15—20° while bromine (29·1 g.) was added slowly. The stirring was continued for 24 hr. at 15—20° and then for 15 min. at 60°. Separation and distillation of the two layers as described above gave 3-bromo-1 : 1 : 1-trifluorobutan-2-one (13·6 g.), b. p. 92—93°, n_D^{20} 1·3790. This sample was shown by analytical gas-liquid partition chromatography [8] to be identical with that described above.

The monobromo-ketone (1·45 g.) was added to a filtered solution of semicarbazide hydrochloride (0·90 g.) and sodium acetate trihydrate (1·35 g.) in water (8 c.c.). After 2 hr. at 0° the *semicarbazone* (1·02 g.) was filtered off and washed with a little cold water. It had m. p. 113—114° (Found: C, 22·55; H, 2·9. $C_5H_7ON_3BrF_3$ requires C, 22·9; H, 2·7%).

3 : 3-*Dibromo-1 : 1 : 1-trifluorobutan-2-one.*—3-Bromo-1 : 1 : 1-trifluorobutan-2-one (17·8 g.), fused sodium acetate (7·8 g.), and glacial acetic acid (65 c.c.) were stirred together at 15—20° while bromine (15·3 g.) was added slowly. The solution was stirred for 7 hr. and kept for 10 hr. at 15—20°, then filtered, and the filtrate was cooled in a cold-water bath and stirred while concentrated sulphuric acid (300 c.c.) was added. The lower layer was separated, washed with concentrated sulphuric acid (50 c.c.), and fractionated (1′ glass-packed column), to give 3 : 3-*dibromo-1 : 1 : 1-trifluorobutan-2-one* (15·2 g.), b. p. 124°, n_D^{22} 1·4302 (Found: C, 17·2; H, 1·4. $C_4H_3OBr_2F_3$ requires C, 16·9; H, 1·1%).

In an alternative preparation, ethyl trifluoromethyl ketone (33·0 g.), fused sodium acetate (45·1 g.), and glacial acetic acid (355 c.c.) were stirred at 15—20° while bromine (88·0 g.) was added during 45 min. The solution was stirred for 5 hr. and then kept for 65 hr. at 15—20°. It was decanted from the solid and treated with concentrated sulphuric acid (1200 c.c.) as described above. Separation and distillation of the lower layer gave the dibromo-ketone (40·1 g.), b. p. 124—125°.

1 : 1 : 1-*Trifluorobutane-2 : 3-dione Dioxime.*—3 : 3-Dibromo-1 : 1 : 1-trifluorobutan-2-one (8·30 g.) was heated for 3 hr. at 100° with hydroxylamine hydrochloride (9·5 g.) and sodium acetate trihydrate (19·0 g.) in water (60 c.c.). The solution was cooled and extracted thrice with ether. The extracts were dried ($MgSO_4$) and concentrated under diminished pressure. The residue (4·14 g.) was recrystallised from benzene, to give 1 : 1 : 1-*trifluorobutane-2 : 3-dione*

[7] Sykes, Tatlow, and Thomas, *J.*, 1956, 835.
[8] Evans and Tatlow, *J.*, 1955, 1184.

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dioxime (1·17 g.), m. p. 89·5—90·5° (Found : C, 28·2; H, 3·0; F, 33·5. $C_4H_3O_2N_2F_3$ requires C, 28·2; H, 3·0; F, 33·5%). The mother-liquors from the recrystallisation were concentrated and the residue distilled under diminished pressure, to give an oil (b. p. 74—76°/0·2 mm.). This solidified partly, giving after filtration and recrystallisation a further quantity of the dioxime (0·4 g.), m. p. and mixed m. p. 88·5—89·5° A semi-solid (1·0 g.) and a viscous liquid (0·7 g.) were left.

The dibromo-ketone (5·67 g.) was heated at 100° for 3 hr. with hydroxylamine hydrochloride (5·5 g.) in 2M-sodium carbonate solution (30 c.c.). Extraction of the solution and treatment as described above gave the same dioxime (0·75 g.), m. p. and mixed m. p. 88·5—89·5°, and a viscous liquid (1·85 g.).

The dibromo-ketone was refluxed with hydroxylamine hydrochloride in methyl alcohol for 8 hr. The solution was diluted with water and extracted with ether. Concentration and distillation of the extracts gave only the dibromo-ketone (80%).

Reaction of 1 : 1 : 1-*Trifluorobutane*-2 : 3-*dione Dioxime with Nickel Ions in Ammoniacal Solutions.*—The crystalline dioxime (m. p. 89°) was dissolved in water and added to a solution of nickel sulphate (6·7 mg. per c.c.) in 0·67N-ammonia. The drab green *nickel derivative* was filtered off, washed with water, and dried at 100°. It was insoluble in carbon tetrachloride, chloroform, and other organic solvents. It was poorly defined and difficult to purify.

A known weight of the precipitate (about 0·065 g.) was digested with potassium sulphate (1·25 g.) and concentrated sulphuric acid (4·5 c.c.) in a Kjeldahl flask.[9] Hydrogen peroxide was added and the solution was boiled until colourless. The solution was diluted with water, and the nickel was precipitated with dimethylglyoxime in the usual way (Found : Ni, 24·4; 24·6. $C_4H_3O_2N_2F_3Ni$ requires Ni, 25·9%).

The semi-solid and viscous liquid products from the oximation described above, when similarly treated with ammoniacal nickel sulphate solution, gave a precipitate, part of which was extracted by chloroform to give a red solution, leaving a drab green precipitate suspended in the aqueous layer.

The dibromo-ketone (2·00 g.) was heated at 100° for 3 hr. with hydroxylamine hydrochloride (2·0 g.) and sodium acetate trihydrate (4·0 g.) in water (10 c.c.). Extraction and distillation in the usual way gave the crude mixed dioxime (1·1 g.). This was dissolved in water and added to an ammoniacal solution of nickel sulphate as described above, and the resulting mixture was extracted with chloroform.

The aqueous layer was acidified with dilute acetic acid and extracted with ether. Concentration of the extracts gave the dioxime (15%), m. p. and mixed m. p. 88—89°, which reacted with nickel ions in ammonia solution to give only the drab green precipitate.

The red chloroform solution was dried ($MgSO_4$) and concentrated, to leave a red *nickel derivative* (0·33 g., 24%) (Found : C, 24·5; H, 2·3; Ni, 14·8. $C_8H_8O_4N_4F_6Ni$ requires C, 24·2; H, 2·0; Ni, 14·8%).

Treatment of the red nickel complex (0·2 g.) with hydrochloric acid and extraction with ether in the usual way gave the dioxime (0·1 g.), m. p. and mixed m. p. 88·5—90·5°, which reacted with an ammoniacal nickel solution to give the drab green precipitate, no red complex being re-formed.

Treatment of the Crude Dioxime Mixture with Hydrochloric Acid.—The dibromo-ketone (1·4 g.) was converted into the crude mixed dioxime in the usual way, and a test sample was treated with ammoniacal nickel sulphate solution as described above. A mixture of the red complex, soluble in chloroform, and the green compound, insoluble in chloroform, was formed.

The crude dioxime was dissolved in hydrochloric acid, and the solution extracted with ether. The extracts afforded in the usual way the crystalline dioxime (0·19 g., 21%), m. p. and mixed m. p. 85—87°, which reacted with nickel ions to give the green compound. No red complex was formed.

Action of Ammonia Solution on the Dioxime.—The dioxime (0·62 g.; m. p. 89°) was heated at 100° for 3 hr. with 2N-ammonia (10 c.c.). Ether-extraction of the solution afforded an unidentified product (0·035 g.) which did not react with nickel ions. Acidification of the aqueous solution with acetic acid and treatment with cerous nitrate solution gave a copious precipitate of cerous fluoride.

Hydrolysis of 1 : 1 : 1-*Trifluorobutane*-2 : 3-*dione Dioxime.*—The dioxime was heated at 100°

[9] Nyholm, *J.*, 1950, 2061.
[10] Rausch, Lovelace, and Coleman, *J. Org. Chem.*, 1956, **21**, 1328.

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for 3 hr. with 5N-hydrochloric acid, and the resulting solution was extracted with ether. The extracts were dried ($MgSO_4$) and concentrated, to leave a residue which could not be purified but was refluxed for 1 hr. with *o*-phenylenediamine in ethyl alcohol. Water was added and the precipitate was filtered off and recrystallised from aqueous ethyl alcohol, to give *2-methyl-3-trifluoromethylquinoxaline*, m. p. 83—84° (Found : F, 26·6. $C_{10}H_7N_2F_3$ requires F, 26·9%).

Reaction of Ethyl Trifluoromethyl Ketone with Selenium Dioxide.—The ketone (10·9 g.) was heated at slightly below the b. p. for 15 hr. with selenium dioxide (12·0 g.) in water (30 c.c.). The aqueous solution was then distilled, to give ethyl trifluoromethyl ketone (4·3 g.) which gave a peak coincident with that from the authentic ketone in gas chromatography.[6] The selenium (3·47 g., 51%) was filtered off and the filtrate was extracted with ether. The extracts were dried ($MgSO_4$) and concentrated and distilled, to give a heterogeneous liquid, b. p. 60—120°.

Part of the distillate (1·0 g.) was heated at 100° for 3 hr. with hydroxylamine hydrochloride (1·1 g.) and sodium acetate trihydrate (2·2 g.) in water (6 c.c.). Ether-extraction and treatment in the usual way gave 1 : 1 : 1-trifluorobutane-2 : 3-dione dioxime (0·13 g.), m. p. and mixed m. p. 87—89°.

The remainder of the distillate, refluxed with *o*-phenylenediamine in ethyl alcohol, gave 2-methyl-3-trifluoromethylquinoxaline, m. p. and mixed m. p. 83—84° (Found : C, 56·9; H, 3·2. Calc. for $C_{10}H_7N_2F_3$: C, 56·6; H, 3·3%).

3 : 3-*Dibromo*-1 : 1 : 1-*trifluoroacetone*.—Trifluoroacetic acid with methylmagnesium iodide (method of Sykes, Tatlow, and Thomas [7]) gave 1 : 1 : 1-trifluoroacetone (57%), which was brominated by McBee and Burton's method [2] giving 3 : 3-dibromo-1 : 1 : 1-trifluoroacetone (61%), b. p. 113°, n_D^{16} 1·4335 (Found : C, 12·8; H, 0·4. Calc. for $C_3HOBr_2F_3$: C, 13·3; H, 0·4%). McBee and Burton [2] gave b. p. 113·3—113·4°/735·5 mm., n_D^{20} 1·4311.

The dibromo-ketone (2·05 g.) was heated at 100° for 1 hr. with semicarbazide hydrochloride (1·75 g.) and sodium acetate trihydrate (2·7 g.) in water (15 c.c.) and then cooled. The solid was filtered off and recrystallised from aqueous ethyl alcohol, to give a disemicarbazone (1·0 g.), m. p. 208—210° (decomp.), which contained no bromine. McBee and Burton [2] gave m. p. 218° (decomp.).

The dibromo-ketone (0·7 g.) was added to a filtered solution of semicarbazide hydrochloride (0·5 g.) and sodium acetate trihydrate (0·75 g.) in water (4 c.c.) at 10—15°. Filtration after 30 min. gave a *semicarbazone* (0·51 g.), m. p. 134·5—135° (decomp.), which contained bromine (Found : C, 14·6; H, 1·6. $C_4H_4ON_3Br_2F_3$ requires C, 14·7; H, 1·2%).

3 : 3 : 3-*Trifluoropyruvaldehyde Dioxime*.—3 : 3-Dibromo-1 : 1 : 1-trifluoroacetone (8·0 g.) was heated at 100° for 90 min. with hydroxylamine hydrochloride (8·2 g.) and sodium acetate trihydrate (16·4 g.) in water (50 c.c.). After extraction with ether the extracts were dried ($MgSO_4$) and concentrated under diminished pressure. Recrystallisation of the residue from benzene gave 3 : 3 : 3-*trifluoropyruvaldehyde dioxime* (2·7 g.), m. p. 117·5—119·5° (Found : C, 22·9; H, 2·2; F, 36·9. $C_3H_3O_2N_2F_3$ requires C, 23·1; H, 1·9; F, 36·5%).

Sensitivities of the Dioximes towards Nickel Ions.—The crystalline trifluorobutanedione dioxime, m. p. 89°, gave precipitates with about 1·5 mg./c.c. or more of Ni^{++} in solutions which were 0·5—0·67N with respect to ammonia. No precipitate was formed even with 6·7 mg./c.c. of Ni^{++} in solutions which were neutral, acidic with acetic acid (0·67N), or more than 0·8N with respect to ammonia.

The sensitivity of the supposed α-form in the oxime residue was not easily determined, but a red precipitate was still formed in solutions containing about 0·5 mg./c.c. of nickel in 0·5N-ammonia.

3 : 3 : 3-Trifluoropyruvaldehyde dioxime gave only a blood-red colour even with 10 mg./c.c. of Ni^{++} in 0·5N-ammonia solution.

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459. *The Mechanism of the Coupling of Diazonium Salts with Heterocyclic Compounds. Part II.* The Reaction of the Neutral Indole Molecule.*

By J. H. Binks and J. H. Ridd.

The reaction of diazonium ions with excess of indole has been studied in very dilute aqueous solution. The kinetics appear to be due to the superposition of two reactions, a normal azo-coupling reaction and an autocatalytic side-reaction that removes diazonium ions but does not form the azo-compound. Over the range pH4—6, the kinetics of the azo-coupling suggest that substitution occurs directly into the neutral indole molecule, and not by previous formation of the conjugate base. No deuterium isotope effect was observed.

Indole reacts readily with weak electrophilic reagents, such as iodine [1] or diazonium ions, in neutral or alkaline media. Monosubstitution occurs, apparently at the 3-position, and more complex products are often also produced. However, this reactivity may not be characteristic of the neutral indole molecule. Indole is a weak acid, and its reactions with electrophilic reagents may occur by the previous formation of the conjugate base; in this, it is sometimes compared with the feebly acidic phenols. The work now reported was carried out to resolve this uncertainty in the mechanism of substitution and to give a measure of the reactivity of the neutral indole molecule.

The colour reaction of indole with diazotised sulphanilic acid has long been known,[2] but few indole azo-compounds have been isolated pure. The reaction of indole with benzenediazonium chloride has been shown to give some 3-phenylazoindole,[3] and that with diazotised arsanilic acid gives an azo-compound that is probably substituted in the same position.[4] The only other well-defined azo-compound is that containing a *p*-bromophenylazo-group, prepared from indole and *p*-bromophenylazoxycarboxamide in alkaline solution.[5] Other azo-compounds have been prepared from substituted indoles.

A kinetic study has been made of the reaction of several diazotised amines with a tenfold excess of indole in aqueous solution at 25°. The solutions used were very dilute, and the reaction was followed by colorimetric estimation of the diazonium ions. At pH 6·68, the reaction with *p*-nitrobenzenediazonium ions obeyed the expected first-order equation, but this was not true of the reactions with the other diazonium ions. The plots of % of reaction against time (see Figure) show that the first-order form is modified by an apparent autocatalysis, and that this modifying term becomes more important as the reactivity of the diazonium ion is decreased. Experiments on the diazo-coupling with sulphanilic acid at different acidities showed that an increased degree of autocatalysis in the disappearance of diazonium ions coincided with a decreased yield of the azo-compound. The autocatalysis therefore arises from some further reaction of the diazonium ions either with the monoazo-compound or with some side product of the primary coupling reaction. In this pH region, the normal decomposition of the diazonium ions is itself partially autocatalysed, owing to coupling with the phenols formed; however this reaction is too slow to explain the autocatalysis observed.

The reaction with *p*-nitrobenzenediazonium ions was chosen for further study because of its simple kinetic form. A pure sample of the monoazo-compound was prepared, and this, by analogy with the derivative from diazotised aniline, is presumed to be 3-*p*-nitrophenylazoindole. The spectrum was studied over a range of acid and alkali concentrations,

* Part I, *J.*, 1953, 3937.

[1] Pauly and Gundermann, *Ber.*, 1908, **41**, 3999.
[2] Ref. 1, footnote, p. 4004.
[3] Madelung and Wilhelm, *Ber.*, 1924, **57**, *B*, 234.
[4] Mingoia, *Gazzetta*, 1930, **60**, 134.
[5] Pieroni, *ibid.*, 1924, **54**, 157.

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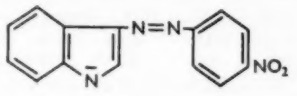
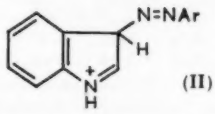
and the results were used to estimate the concentration of azo-compound formed in the kinetic experiments. The spectrum shows a marked change in alkaline solution, presumably owing to proton loss to form the 1-indolyl anion (I).

(I)  (II) 

The yield of 3-*p*-nitrophenylazoindole as a function of pH is shown in Table 1; between pH 4 and 6 the yield is almost quantitative. These values were obtained by making the reaction mixture alkaline and comparing the spectrum with that of the 1-indolyl anion (I).

The kinetics of the reaction of indole with *p*-nitrobenzenediazonium ions were then studied in this pH range at 0°. Most of these kinetic runs were followed from the concentration of the azo-compound, but some were followed from the concentration of the diazonium ions; the two methods were in good agreement. A large excess of indole was used, and, as expected, the results fitted a first-order equation. This indicates that the reaction is of first order with respect to diazonium ions.

Reaction of diazonium ions with indole, as followed from the concentration of diazonium ion.

$[C_8H_7N] = 2{\cdot}5 \times 10^{-4}$. $[ArN_2^+] = 2{\cdot}5 \times 10^{-5}$.
pH = 6·68. Temp. = 25°.
A = p-*Nitroaniline*. *C* = *Sulphanilic acid*.
B = p-*Chloroaniline*. *D* = *Aniline*.

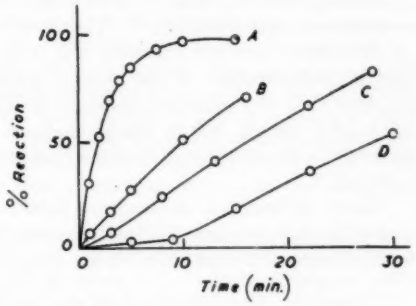


TABLE 1. *Yield of* p-*nitrophenylazoindole under conditions of kinetic experiments.*

$[C_8H_7N] = 5 \times 10^{-4}$M. $[ArN_2^+] = 25 \times 10^{-6}$M.

pH *	2·0	2·9	3·3	3·78	5·21	5·69	6·17	6·78	7·07	7·61
Yield, %	25·6	44·8	74·5	94·7	98·5	97·6	96·7	74·7	60·0	36·4

* All pH measurements were at 25°.

TABLE 2. *Determination of order with respect to indole.*

pH = 3·78. $[ArN_2^+] = 25 \times 10^{-6}$. Temp. = 0°.

$10^4[C_8H_7N]$	1·25	2·5 *	5·0 *	5·0	10·0
10^4k_1 (sec.$^{-1}$)	3·04	6·3	11·1	11·3	26·1
k_2 (sec.$^{-1}$ mole^{-1} l.)	2·43	2·52	2·22	2·26	2·61

* These runs were followed from the concentration of diazonium-ion, the others from the concentration of azo-compound.

The first-order rate coefficients (k_1) for some of the kinetic runs are listed in Table 2, together with the second-order rate coefficients (k_2) obtained by dividing k_1 by the stoicheiometric concentration of indole in the solution. The results in Table 2 show that k_2 is effectively constant over an eight-fold increase in the indole concentration; the reaction is therefore of first order with respect to indole. The results in Table 3 show that this second-order rate coefficient varies only slightly over the pH range 3·78—6·17; over this range therefore, the kinetic equation does not also contain a pH-dependent term. The

full kinetic equation is therefore rate $= k_2[C_8H_7N][ArN_2^+]$, where the concentration terms refer to the analytical or stoicheiometric concentrations of the reactants.

TABLE 3. *Variation of the second-order rate coefficient (in l. sec.$^{-1}$ mole^{-1}) with* pH.

$[C_8H_7N] = 5 \times 10^{-4}$. $[ArN_2]^+ = 25 \times 10^{-6}$. Temp. = 0°.

pH	3·78	4·55	4·87	5·21	5·69	6·17	6·68	6·78	7·61	8·60	9·20
k_2	2·26	2·24	2·18	2·20	2·08	2·04	3·10*	3·16*	3·90*	5·20*	4·50*

All runs were followed from the concentration of azo-compound.
* These are approximate initial values; see text.

However, from the equilibrium constants for the diazo-equilibria,[6] and from the estimated basicity of indole,[7] it follows that, in this pH range, the actual concentrations of diazonium ions and indole molecules are both equal to their stoicheiometric values; the equation is therefore also thus when the concentration terms refer to the actual chemical species.

Much evidence suggests that diazonium ions are the effective electrophilic reagents in aqueous diazo-couplings.[8] The equation is clearly consistent with the direct reaction of diazonium ions with indole, and inconsistent with the prior formation of an equilibrium concentration of the indolyl anion. Hence, in these feebly acidic solutions, it appears that the observed reaction is due to the neutral indole molecule. Comparison with other kinetic results shows that, on a logarithmic scale, the reactivity of the indole molecule is about midway between that of the 1-naphthoxide ion and the neutral 1-naphthol molecule.[9]

More evidence on the reaction path is obtained by comparing the reactivity of indole and of 3-deuteroindole. Kinetic results for the reaction of *p*-nitrobenzenediazonium ions with indole and 3-deuteroindole are shown in Table 4; they indicate that the rate difference

TABLE 4. *Comparison of the azo-coupling of indole and 3-deuteroindole with* p-*nitrobenzenediazonium ions at* 0°.

$[C_8H_7N] = 5 \times 10^{-4}$. $[ArN_2^+] = 27{\cdot}7 \times 10^{-6}$. pH = 6·68.

	Time (min.)	1	2	3	4	5	10
Indole	10^6[azo-cpd.]	2·7	5·3	7·3	9·1	10·7	16·8
	10^4k_1 (sec.$^{-1}$)	16·9	17·6	16·9	16·5	16·2	15·5
3-Deuteroindole	10^6[azo-cpd.]	3·1	5·3	7·2	8·9	10·6	16·4
	10^4k_1 (sec.$^{-1}$)	19·6	17·6	16·6	16·1	16·1	15·0

is slight and probably within the experimental error. This implies that the C–H and C–D bonds are not appreciably stretched in the rate-determining step; it therefore excludes the possibility that the ion (II) is formed in equilibrium concentration and then undergoes a slow rate-determining loss of a proton to a water molecule. The diazo-coupling of indole is therefore similar to that of the homocyclic compounds where, in the absence of steric hindrance, a slow attack of the diazonium ion is followed by a rapid loss of proton.[10]

Kinetic studies at higher values of pH are complicated by the partial conversion of the diazonium chloride into the diazo-hydroxide and the alkali diazoate. Since the diazonium ions are the only effective electrophilic reagent in diazo-coupling,[11] this shift in equilibrium concentration should reduce the rate of the coupling reaction. Also, with *p*-nitrobenzenediazonium ions, the yield of the azo-compound is decreased (Table 1). Nevertheless the initial rate of formation of the azo-compound is at first increased as the pH is raised above 6·2. This is shown by the second group of runs in Table 3. The second-order rate coefficients are the values of the mean rate of formation of the azo-compound during the first two minutes divided by the initial concentration of diazonium

[6] Grachev, *Zhur. obshchei Khim.*, 1947, **17**, 1834.
[7] Albert, Goldacre, and Phillips, *J.*, 1948, 2240.
[8] Zollinger, *Chem. Reviews*, 1952, **51**, 347.
[9] *Idem, Helv. Chim. Acta*, 1953, **36**, 1070; see also J. H. Binks, Ph.D. Thesis, Univ. of London, 1956.
[10] Zollinger, *Experientia*, 1956, **12**, 165.
[11] Wittwer and Zollinger, *Helv. Chim. Acta*, 1954, **37**, 1954.

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ion and by the concentration of indole. This method of calculation underestimates the initial rate coefficients, nevertheless the increase over the previous values is unmistakable. The experiments on 3-deuteroindole show that this rate increase cannot be due to assisted loss of proton in the transition state; it is therefore likely to arise from an alternative reaction path involving the conjugate base of indole.

Experimental

Samples of indole were purified immediately before use by sublimation *in vacuo*; the purified material had m. p. 52°. The amines were either recrystallised or distilled before use. The buffer reagents and the sodium nitrite were "AnalaR"; the latter was recrystallised twice from water and dried. Throughout the following account, the solvent was water, unless otherwise stated.

Kinetics.—When the kinetic runs were followed colorimetrically from the concentration of diazonium ion, the procedure was essentially as described in Part I, except that the concentration of hydrochloric acid during the diazotisation was 0·4N, and that 3-hydroxynaphthalene-2 : 7-disulphonic acid was used as the coupling reagent. The concentration of diazonium ions was determined before each kinetic run and this value was used in the calculations.

When the runs were followed from the concentration of azo-compound, a series of separate reaction mixtures was prepared from the same diazonium-ion solution. After an appropriate time, the reaction was stopped by adding a solution of potassium hydroxide in aqueous ethanol. The concentrations were adjusted so that the final concentration of potassium hydroxide was 0·1M in 50% ethanol by volume. The concentration of azo-compound was calculated by comparing the optical density of this solution with that of solutions of the pure azo-compound in the same medium.

Conventional buffering agents (phthalate, phosphate, or borate) were used in the kinetic runs, the combined concentration of the buffer acid and the conjugate base being 0·05—0·1M. The results suggest that the reaction rate is not very sensitive to the nature or concentration of the buffer solution.

Preparation of 3-Deuteroindole.—In the pH range 2·5—0·5, it has been shown that the 1- and the 3-hydrogen atom of indole can be exchanged with the deuterium of heavy water; at higher pH values only the 1-hydrogen atom can be exchanged.[12] 3-Deuteroindole was therefore prepared as below.

A suspension of indole (1 g.) in a mixture of heavy water (99·78%; 10 ml.) and deuterated hydrochloric acid (0·1N; 1 ml.) was stirred for 4 hr. at 60°. The indole was recovered by extraction with ether, and the process was repeated twice with fresh deuterating solutions. The deuterium atom at position 1 was then removed by treatment with potassium hydrogen phthalate solution (M/20; pH 4). After purification of the indole by sublimation, the analysis of the hydrogen produced by combustion and reduction corresponded to 93·1% exchange at a single position.

Preparation of the Azo-compounds.—*p*-Nitroaniline (3 g.) in dilute hydrochloric acid (325 ml.; 0·9N) was diazotised at 0° with sodium nitrite (2·5 g.) and added slowly to indole (2 g.) in dilute potassium hydroxide (5 g. of KOH in 800 ml. of water) containing crushed ice (200 g.). The red precipitate was dried (yield, 1·4 g.). Part of this was dissolved in benzene and chromatographed on alumina. After elution with benzene containing 5% of ethanol, the main orange band was separated and extracted with ethanol. Water was added to the ethanol solution, the minute red crystals were filtered off, the compound was again chromatographed, and the product crystallised from ethanol–water. The crystals had m. p. 195—197° (Found : C, 62·6; H, 3·7; N, 20·7. Calc for $C_{14}H_{10}N_4O_2$: C, 63·2; H, 3·8; N, 21·1%).

3-Phenylazoindole was prepared as above : it had m. p. 134—135° (Found : C, 76·1; H, 5·0; N, 18·6. Calc. for $C_{14}H_{11}N_3$: C, 75·9; H, 5·0; N, 19·1%). The mono-azo-compound from *p*-chloroaniline was similarly prepared except that the potassium hydroxide was omitted and the final crystallisation was from benzene. The product had m. p. 179—181° (Found : C, 65·8; H, 4·1; N, 17·1; Cl, 14·6. Calc. for $C_{14}H_{10}N_3Cl$: C, 65·7; H, 3·9; N, 16·4; Cl, 13·9%).

Spectra of the Azo-compounds.—In aqueous dioxan or aqueous ethanol, these compounds give a yellow solution. When the solutions are made alkaline, that of the *p*-nitrophenylazo-compound becomes purple, that of the *p*-chlorophenylazo-compound becomes pale orange

[12] Koizumi and Titani, *Bull. Chem. Soc. Japan*, 1938, **13**, 307.

(but in a higher alkali concentration), and that of 3-phenylazoindole is unaffected. This order is as expected if the change is due to loss of proton.

These azo-compounds (as the neutral molecules) have one absorption maximum at about 280 mμ and a stronger maximum nearer the visible region. Ionisation increases the intensity of this second maximum and causes a marked shift to longer wavelengths. The spectra of 3-*p*-nitrophenylazoindole solutions were studied at different concentrations of hydroxide ion in 50% aqueous ethanol. The solutions obey Beer's law and have an isosbestic point at 482 mμ ($\varepsilon_\lambda = 1{\cdot}32 \times 10^4$); the ionisation appears to be almost complete when the stoicheiometric concentration of hydroxide ions is 0·05M. In contrast, 3-*p*-chlorophenylazoindole is not fully ionised when the concentration of hydroxide ion is 1·0M. Details of the main absorption maxima are summarised below.

Indole	Medium	$[OH^-]$ *	$\lambda_{max.}$, mμ	$10^{-4}\varepsilon$
3-*p*-Nitrophenylazo-	50% aq. ethanol †	—	440	2·11
,, ...	,,	0·05	550	3·56
3-*p*-Chlorophenylazo-	,,	—	372	2·66
,, ...	,,	1·0	446	3·24
3-Phenylazo-	5% dioxan–95% water †	—	368	1·61

* Stoicheiometric concentration. † By volume.

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460. *Researches on Ammines. Part XI.** cis-*Nitroaquotetramminocobaltic Salts.*

By H. J. S. King and S. N. Mistry.

Sulphatoaquotetramminocobaltic chloride with one equivalent of silver nitrite gave nitroaquotetramminocobaltic sulphate. The derived chloride, bromide, and nitrate have been obtained. These salts differ considerably from the nitroaquotetramminocobaltic salts described by previous workers. It is concluded that the salts now described have the *cis*-configuration, while those described previously are *trans*-compounds.

Nitroaquotetramminocobaltic salts were discovered by Jörgensen.[1] By heating *trans*-dinitrotetramminocobaltic sulphate with concentrated hydrochloric acid, he obtained brownish-red chloronitrotetramminocobaltic chloride, which on recrystallisation yielded a red salt regarded as nitroaquotetramminocobaltic chloride, $[Co(NH_3)_4(H_2O)(NO_2)]Cl_2$. From the chloride, a yellow nitrate and sulphate and a red bromide were obtained. Werner[2] showed that the yellow salts are true nitroaquotetrammines but that the red salts should be formulated $[Co(NH_3)_4(NO_2)Hal]Hal,H_2O$. Werner prepared the true nitroaquotetramminocobaltic chloride and bromide which were yellow but changed rapidly to the red isomers. Chloronitro- and nitroaquo-tetramminocobaltic salts may be expected to exist in *cis*- and *trans*-forms, but in each case only one series has hitherto been recorded. Meyer and Gröhler,[3] by treating $[Co(NH_3)_4(NO_2)Cl]Cl$ with concentrated selenic acid, obtained not a selenato-salt $[Co(NH_3)_4(SeO_4)]X$, but a dihydroselenato-salt, $[Co(NH_3)_4(HSeO_4)_2]X$, where X is a univalent acid radical: this was considered to indicate a *trans*-structure for the chloronitrotetrammine, since the *cis*-compound would be expected to yield the selenato-salt. The chloronitrotetrammines undergo immediate aquation in

* Part X, *J.*, 1948, 1912.

[1] Jörgensen, *Z. anorg. Chem.*, 1894, **7**, 289.
[2] Werner, *Ber.*, 1907, **40**, 4124.
[3] Meyer and Gröhler, *Z. anorg. Chem.*, 1926, **155**, 91.

cold water to nitroaquotetrammines, so the latter were also considered to have the *trans*-configuration. Meyer and Rampoldt [4] prepared both *cis*- and *trans*-nitroaquobisethylenediaminecobaltic salts: the orange *cis*-salts were very soluble and did not crystallise, while the brown *trans*-salts were less soluble and crystallised well. This supported the view that the known series of nitroaquotetramminocobaltic salts, being difficultly soluble and well crystalline, have *trans*-structures.

Ephraim and Flugel [5] were unable to isolate $[Co(NH_3)_4(H_2O)(SO_4)]I$, owing to its rapid conversion into $[Co(NH_3)_4(H_2O)I]SO_4$, so it appeared likely that the nitrite of the sulphatoaquotetramminocobaltic series would undergo a similar change, in view of the strong tendency of the nitrite ion to enter the complex, at the same time changing to the nitro-group. This was found to be the case, and the sulphate of a new series of nitroaquotetramminocobaltic salts has now been obtained, by treating sulphatoaquotetramminocobaltic chloride with one molecular proportion of silver nitrite. The filtrate yielded a light brown amorphous powder, the solution of which gave an immediate precipitate with barium chloride in the cold and very little further precipitate on boiling. No oxides of nitrogen were evolved, even with concentrated hydrochloric acid. Thus the product had undergone practically complete conversion into nitroaquotetramminocobaltic sulphate:

$$[Co(NH_3)_4(H_2O)(SO_4)]O{\cdot}NO \longrightarrow [Co(NH_3)_4(H_2O)(NO_2)]SO_4$$

By treating the sulphate with the calculated amounts of barium chloride, bromide, or nitrate, the chloride, bromide, and nitrate of the new series were obtained, as very soluble brown amorphous powders which gave no oxides of nitrogen on acidification. In addition to their much greater solubility, the properties of these salts differed notably from those of the nitroaquotetrammines described by Jörgensen [1] and Werner.[2] The chloride and bromide were stable, alone and in presence of water, whereas Werner's salts changed on storage, and more rapidly in water, to the isomeric red compounds, $[Co(NH_3)_4(NO_2)Hal]Hal,H_2O$.

Werner found that nitroaquotetramminocobaltic nitrate dissolved in aqueous ammonia to a red solution which deposited red crystals of the corresponding nitrohydroxo-salt on cooling:

$$[Co(NH_3)_4(H_2O)(NO_2)](NO_3)_2 \longrightarrow [Co(NH_3)_4(OH)(NO_2)]NO_3$$

The brown nitroaquotetrammines now described also gave red solutions in aqueous ammonia but it was only possible to isolate the brownish-yellow hydroxonitrotetrammines in very small yield, owing to their high solubility.

If it is accepted that the previous nitroaquotetrammines obtained are *trans*-compounds, the salts now described must be given the *cis*-configuration, and this is supported by the preparation of the new series from sulphatoaquotetramminocobaltic chloride, which is shown to be a *cis*-compound (see below).

The water molecule in the complex of the new series was removed completely at 110°, without loss of ammonia. The substance produced by dehydration of the sulphate was presumably $\left[Co(NH_3)_4(NO_2)\begin{matrix}O\\ \diagdown\\ S\\ \diagup\\ O\end{matrix}\!\!\begin{matrix}O\\ \diagup\\ \diagdown\\ O\end{matrix}\right]^{+}O^{-}$ in which the sulphate radical may be regarded as a "bound ion." Dehydration of the chloride and bromide may be expected to yield *cis*-$[Co(NH_3)_4(NO_2)Hal]Hal$, differing from the nitroaquo-salts in having only half the chlorine or bromine in the ionised condition. This was tested experimentally in the case of the nitroaquo-bromide. Before dehydration, the whole of the bromine was precipitated forthwith in the cold by silver nitrate. From a cold solution of the dehydrated salt, three-quarters of the total bromine was precipitated immediately, and the filtrate yielded the remainder on boiling. Evidently the bromonitro-bromide was partially reconverted into the original nitroaquo-bromide in aqueous solution.

[4] Meyer and Rampoldt, *Z. anorg. Chem.*, 1933, **214**, 1.

The configuration of the sulphatoaquotetramminocobaltic complex was investigated by treating the chloride of the series with one molecular proportion of barium nitrite. The filtrate yielded brown crystals of *cis*-dinitrotetramminocobaltic chloride, indicating that the original sulphatoaquo-salt also had the *cis*-configuration.

Experimental

Configuration of the Sulphatoaquotetramminocobaltic Complex.—Sulphatoaquotetramminocobaltic chloride was prepared by Ephraim and Flugel's method.[5] This salt (2 g.) was shaken mechanically with barium nitrite (1 mol.) and water (20 ml.), and the barium sulphate was removed by centrifuging. The red solution, when treated with ethanol (75 ml.) and ether (20 ml.), yielded very soluble brown microscopic crystals which were dried in a vacuum over magnesium perchlorate {Found : Co, 23·1; NH_3, 26·8; Cl, 13·9. $[Co(NH_3)_4(NO_2)_2]Cl$ requires Co, 23·1; NH_3, 26·8; Cl, 13·9%}. The solution gave a pink precipitate with ammonium oxalate (distinction from *trans*-dinitrotetrammines). The colour and high solubility of the chloride and the insolubility of the oxalate indicate that the salt obtained was the cis-*compound*.

cis-*Nitroaquotetramminocobaltic Sulphate.*—Sulphatoaquotetramminocobaltic chloride (2 g.), silver nitrite (1 mol.), and water (20 ml.) were shaken for 1 hr., and the deep-red filtrate was taken to dryness in a vacuum over sulphuric acid. The brown amorphous product (1·5 g.) was only moderately soluble (1 : 30 at 15°). It did not yield oxides of nitrogen when heated with hydrochloric acid. 88% of the sulphate radical was immediately precipitated in the cold by barium chloride, the remainder being precipitated on boiling (the first precipitate was separated by centrifuging) {Found : Co, 20·6; NH_3, 23·7; N, 24·4; SO_4, 33·4; H_2O (lost in 8 hr. at 100°), 6·2. $[Co(NH_3)_4(H_2O)(NO_2)]SO_4$ requires Co, 20·5; NH_3, 23·7; N, 24·4; SO_4, 33·5; H_2O, 6·5%}. The *nitroaquo-sulphate* (1 g.) was dissolved in the minimum amount (40 ml.) of 3N-ammonia at 50°; when the red solution was strongly cooled, the *product* separated as a scanty brownish-yellow amorphous powder (0·1 g.) {Found : Co, 24·8. $[Co(NH_3)_4(OH)(NO_2)]_2SO_4$ requires Co, 24·7%}.

cis-*Nitroaquotetramminocobaltic chloride* was obtained when the sulphate (1 g.) was shaken for 1½ hr. with hydrated barium chloride (1 mol.) and water (30 ml.). The solution, after removal of barium sulphate by centrifuging, was taken to dryness in a vacuum over sulphuric acid, and yielded the nitroaquo-chloride (0·7 g.) as a very soluble light-brown amorphous powder. Water in the complex was almost completely removed in 6 hr. at 110°, no ammonia being lost, the colour then being buff {Found : Co, 22·5; NH_3, 25·9; N, 26·7; Cl, 27·0; H_2O, 6·3. $[Co(NH_3)_4(H_2O)(NO_2)]Cl_2$ requires Co, 22·5; NH_3, 25·9; N, 26·7; Cl, 27·0; H_2O, 6·8%}.

cis-*Nitroaquotetramminocobaltic Bromide.*—The sulphate (2 g.) was shaken for 1½ hr. with anhydrous barium bromide (2·07 g.) and water (30 ml.). After centrifuging, the brown solution was cooled in ice and treated with ethanol (100 ml.) and ether (100 ml.). The *bromide* separated as a very soluble brown amorphous powder (2 g.) and was kept overnight in a vacuum over magnesium perchlorate. Water in the complex was completely removed, without loss of ammonia, in 9 hr. at 100°, thus yielding a buff powder {Found : Co, 16·8; NH_3, 19·4; N, 20·2; Br, 45·1; H_2O, 5·1. $[Co(NH_3)_4(H_2O)(NO_2)]Br_2$ requires Co, 16·8; NH_3, 19·4; N, 19·9; Br, 45·5; H_2O, 5·1%}. When treated with silver nitrate, a solution of the dehydrated salt (0·139 g.) gave an immediate precipitate of silver bromide (0·1176 g.) and a further precipitate (0·0391 g.) on boiling.

cis-*Nitroaquotetramminocobaltic Nitrate.*—The sulphate (1 g.) was shaken for 1½ hr. with barium nitrate (0·91 g.) and water (30 ml.). After centrifuging, the solution was taken to dryness in a vacuum over sulphuric acid, and yielded a brown amorphous very soluble powder (0·9 g.) {Found : Co, 18·7; NH_3, 21·6; N, 31·1. $[Co(NH_3)_4(H_2O)(NO_2)](NO_3)_2$ requires Co, 18·7; NH_3, 21·6; N, 31·1%}. This *nitrate* (1 g.) dissolved in 3N-ammonia (7 ml.) at 50° to a red solution. Cooling and adding methanol gave a scanty brownish-yellow microcrystalline precipitate (0·17 g.), very soluble, to a strongly alkaline solution; this was probably *cis*-$[Co(NH_3)_4(OH)(NO_2)]NO_3$.

The Northern Polytechnic, London, N.7. [*Received, December* 31*st*, 1956.]

[5] Ephraim and Flugel, *Helv. Chim. Acta*, 1924, **7**, 724.

461. *Chemical Constitution and the Dissociation Constants of Monocarboxylic Acids. Part XVII.** ortho-*Effects in Substituted Salicylic Acids.*

By L. G. Bray, J. F. J. Dippy, S. R. C. Hughes, and L. W. Laxton.

The dissociation constants of nine substituted salicylic acids have been determined together with those of 3-hydroxy-2-naphthoic acid and its methyl ether. The dissociation constants of salicylic acid and its *meta*- and *para*-isomers have also been measured for the first time by a modern conductometric procedure. The evidence suggests that in the 6-substituted salicylic acids the measured strength is an outcome of competing *ortho*-effects; it appears that the secondary steric effect, imposed by the 6-nitro-substituent, suppresses the internal hydrogen bond involving the carboxyl and hydroxyl groups.

The strength of salicylic acid (in water at 25°) is anomalously high compared with the strengths of the isomeric *m*- and *p*-hydroxybenzoic acids and with those of its methyl and phenyl ethers (as shown by the values of K/K_u, where K_u is the dissociation constant of benzoic acid, in Table 1 [1]—all obtained in this Series).

Table 1. *Values of* K/K_u *for* $X{\cdot}C_6H_4{\cdot}CO_2H$.

X = *o*-OH, 16·1;	*m*-OH 1·32;	*p*-OH, 0·471
X = *o*-OMe, 1·28;	*m*-OMe 1·30;	*p*-OMe, 0·539
X = *o*-OPh, 4·74;	*m*-OPh 1·79;	*p*-OPh, 0·479

To account for the extraordinary dissociation constant of salicylic acid, Branch and Yabroff [2] suggested that an internal hydrogen bond is formed between the carboxyl and hydroxyl groups which stabilises the anion much more than the undissociated acid, so disturbing the equilibrium in favour of dissociation. Additional hydrogen bonding is possible in 2 : 6-dihydroxybenzoic acid, and hence the further large increase in strength ($K/K_u = 830$). More recently, Ingold [3] has suggested that the acid-strengthening influence is due to the introduction of a positive charge into the carboxyl group as a result of the hydrogen bonding which arises partly from electrostatic attraction of the adjacent groups and partly through covalent interaction of these substituents.

The dissociation constants of 3-hydroxy-2-naphthoic acid and its methyl ether (Table 2) again show a remarkably high relative strength for the hydroxy-acid. In fact the situation encountered in the benzene system is reproduced; this is best shown by the results for the relative strengths (K/K_u) where K_u is the strength of the parent acid in each case, *viz.*: salicylic, 16·1; *o*-methoxybenzoic, 1·28; 3-hydroxy-2-naphthoic, 28·4; 3-methoxy-2-naphthoic 2·23.

The nitrosalicylic acids examined display a particularly interesting series of strengths. The most striking fact is that 6-nitrosalicylic (CO_2H is at position 1) is weaker than *o*-nitrobenzoic acid ($10^3K = 6{\cdot}71$), which implies that the specific hydrogen bond operating in salicylic acid (and in its anion in particular) is absent from it. This can be understood on assumption that the O···H–O bridge in the anion (I) requires coplanarity with the benzene ring for its creation.

The nitro-group is like carboxyl in that both groups have $-I$, $-M$ polar characteristics and similar steric requirements. However, the nitro-group is doubtless the more strongly conjugated with the benzene ring (see Part XV), and hence when the two substituents are adjacent their conflicting bulks twist the carboxyl rather than the nitro-group out of the plane of the ring, with the resultant enhancement of strength exhibited by *o*-nitrobenzoic

* Part XVI, *J.*, 1957, 265.

[1] Dippy, *Chem. Rev.*, 1939, **25**, 151.
[2] Branch and Yabroff, *J. Amer. Chem. Soc.*, 1934, **56**, 2568.
[3] Ingold, "Structure and Mechanism in Organic Chemistry," Bell, London, 1953, p. 749.

XUM

acid. It follows, then, that when a substantial group such as nitro is introduced into the 6-position of benzoic acid it will so alter the steric conformation of the carboxyl group that a hydrogen-bridge is no longer formed when hydroxyl enters the 2-position. The hydroxyl group which, being small, exercises very little bulk obstruction, will then have the net effect of depressing acid strength through the normal internal electromeric displacements ($+M$), in much the same way as it does in *p*-hydroxybenzoic acid ($10^5K = 2{\cdot}9$; cf. benzoic acid $10^5K = 6{\cdot}27$).

The near identity of the strengths of 4-nitro- and 6-nitro-salicylic acids is quite fortuitous; the 4-nitro-acid is an orthodox salicylic acid into which introduction of a

TABLE 2. *Dissociation constants* (10^3K).

Acid	This paper	Earlier values	M. p.	Acid	This paper	Earlier values	M. p.
3-Nitrosalicylic	13·4	15·7 [a,b]	146·5—147°	5-Chlorosalicylic	2·35	1·97 [d]	165°
4-Nitrosalicylic	5·88	—	235—236	6-Chlorosalicylic	2·36	—	171·3—172·3
5-Nitrosalicylic	7·57	8·00 [b]	232—233	5-Bromosalicylic	2·44	—	170—171
		8·90 [c]		6-Methylsalicylic	0·478	0·295,[e] 1·06 [f]	171·3—171·8
6-Nitrosalicylic	5·81	—	166—167				
3 : 5-Dinitrosalicylic	201	—	172—172·5	3-Hydroxy-2-naphthoic	1·96	—	224
				3-Methoxy-2-naphthoic	0·15	—	134—135

[a] Ostwald, *Z. phys. Chem.*, 1887, **1**, 61; 1889, **3**, 260. [b] Magnanini, *Gazzetta*, 1891, **21**, 215. [c] Ostwald, *Z. phys. Chem.*, 1889, **3**, 241, 260. [d] Coppadoro, *Gazzetta*, 1902, **32**, 542. [e] Peltier, *Compt. rend.*, 1955, **241**, 1467 (in 1% aqueous alcohol solution). [f] Stohmann and Langbein, *J. prakt. Chem.*, 1894, **50**, 389.

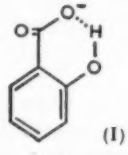
TABLE 3. *Dissociation constants* (10^5K).

Acid	This paper	Earlier values	M. p.
o-Hydroxybenzoic (salicylic)	101	105,[a] 107 [b]	159—159·5°
m-Hydroxybenzoic	8·27	8·3,[a] 8·71 [b]	197—198
p-Hydroxybenzoic	2·95	2·9,[a] 3·31 [b]	217

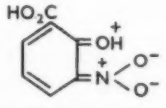
[a] Ref. 2. [b] Kuhn and Wassermann, *Helv. Chim. Acta*, 1928, **11**, 31.

4-nitro-group simply produces its expected acid-strengthening effect, giving only about 2% deviation from the additivity principle discussed in Part XV.[4]

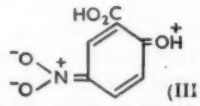
The fact that 3-nitro- and 5-nitro-salicylic acids are stronger than 4-nitrosalicylic acid is a special feature of this series. A nitro-group at the *para*-position with respect to carboxyl in an aromatic acid normally enhances the strength more than when it occupies the *meta*-position (cf. K/K_0 for *m*-nitro- and *p*-nitro-benzoic acids, 5·12 and 5·90 respectively). This is due to the ready operation of the $-M$ effect when the nitro-group is in effective



(I)



(II)



(III)

conjugation. The converse of this feature in the salicylic series can be attributed to the increased polarity of the bond between hydrogen and oxygen in the hydroxyl group brought about by the resonance interaction of hydroxyl with the nitro-group at the *ortho*- or *para*-position with regard to it, as illustrated in the structures (II) and (III) (a possibility denied to the 4-nitrosalicylic acid system). This means that the hydroxyl group can more readily participate in the hydrogen bridge, particularly of the anion, in the cases of the 3- and the 5-nitro-acids [a trend which bestows additional stabilisation on the anion, leading to a larger K (21% and 8% in excess of additivity)] than in that of the 4-nitro-acid (0·3% departure from additivity). The further enhancement of strength shown by 3 : 5-dinitrosalicylic acid, although very great (i.e., +33% departure from additivity), lends emphasis to this interpretation. Any tendency to hydrogen bonding between the

[4] Dippy, Hughes, and Laxton, *J.*, 1956, 2995.

hydroxyl and the nitro-group in 3-nitrosalicylic acid is apparently of secondary significance. It is noteworthy that 3- and 5-nitrosalicylic acids are the only disubstituted benzoic acids treated by us so far which show a large *positive* deviation from additivity, a fact which indicates that a special kind of anomaly operates here.

The strengths of 6-methyl- and 6-chloro-salicylic acids have also been determined. The strength is much less enhanced in each case than expected on the additivity principle as the following departures show: 6-methylsalicylic, −41%; 6-chlorosalicylic, −36%; cf. 6-nitrosalicylic, −39%. Clearly the two substituents at the *ortho*-positions are again unable to exert the influences possible when present independently in benzoic acid; their simultaneous presence seems to inhibit formation of the hydrogen bridge.

Several potentiometric determinations of the approximate strengths of monosubstituted *o*-methylbenzoic acids were made recently by Peltier [5] (in water containing 1% of ethanol) who records pK 3·07, 3·53, and 3·98 respectively for salicylic, 6-methylsalicylic, and *o*-toluic acids. This sequence is consistent with our findings. Peltier observes that this order signifies an important modification of the hydrogen bond in 6-methylsalicylic acid.

It is noteworthy that the strengths of 5-chloro- and 5-bromo-salicylic acids are almost the same and approximately that of 6-chlorosalicylic acid; probably the hydrogen-bridge is strengthened in the 5-halogeno-salicylic acids by the inductive influence of halogen (−I) situated in the *para*-position to the hydroxyl group, thereby enhancing the dissociation constant.

The strengths of the monohydroxy-benzoic acids (Table 3) have now been determined by a modern conductometric procedure and the values of K obtained confirm the lower values of the many to be found in the literature.

Experimental

Materials.—*6-Chlorosalicylic acid.* 2-Chloro-6-nitrotoluene (5 g.) when refluxed with aqueous alkaline permanganate for 5 hr. gave 2-chloro-6-nitrobenzoic acid (3·5 g.) which upon reduction (ferrous sulphate and aqueous ammonia) yielded 2-amino-6-chlorobenzoic acid (2·3 g.). When diazotised, gently warmed, and set aside, this (4·4 g.) gave 6-chlorosalicylic acid, m. p. 164° (Cohn [6] records m. p. 166°).

6-Methylsalicylic acid was similarly prepared [7] from 2-methyl-6-nitrobenzoic acid (obtained by Gabriel and Thieme's method).[8]

4-Nitro- and 6-nitro-salicylic acids were kindly supplied by Dr. A. A. Goldberg of Ward, Blenkinsop and Co., Ltd., and 3-methoxy-2-naphthoic acid by Dr. K. Kerridge whom we thank. The remaining acids were purchased.

Acids were recrystallised from conductivity water, except for 3-hydroxy- and 3-methoxy-2-naphthoic acids which were recrystallised from aqueous acetone and benzene–light petroleum (b. p. 60—80°) respectively. Final specimens were dried in desiccators for two weeks and equivalents confirmed by alkalimetry.

Table 4.

o-*Hydroxybenzoic acid* (*salicylic acid*)			m-*Hydroxybenzoic acid*			p-*Hydroxybenzoic acid*		
10^3c	Λ	10^5K	10^3c	Λ	10^5K	10^3c	Λ	10^5K
4·634	145·5	101	2·561	61·23	8·29	4·187	30·24	$2·92_8$
4·293	149·8	101	2·129	66·29	8·23	2·997	35·47	2·93
1·595	210·1	102	1·790	71·77	8·28	2·307	40·18	$2·94_5$
1·149	232·2	102	1·488	77·71	8·24	1·843	44·67	2·95
0·7973	255·2	102	1·374	80·65	8·29	1·455	49·89	$2·95_5$
0·4057	294·7	100	1·114	88·33	8·29	0·8775	62·83	$2·95_5$
	$\Lambda_0 = 385·2$		0·8458	98·87	8·22	0·7530	67·31	$2·95_5$
			0·6071	114·0	8·33	0·2909	101·3	$2·92_5$
			0·2916	151·0	8·26		$\Lambda_0 = 372·2$	
				$\Lambda_0 = 367·1$				

[5] Peltier, *Compt. rend.*, 1955, 58.
[6] Cohn, *Mitt. Technol. Gewerb.-Mus. Wien*, **11**, 178; *Chem. Zentr.*, 1901, II, 925.
[7] Asahina and Kondo, *J. Pharm. Soc. Japan*, 1922, Nr. 482, S. 3.
[8] Gabriel and Thieme, *Ber.*, 1919, **52**, 1079.

The specific conductance of the water employed was 0·5—0·8 gemmho.

Conductivity Measurements.—Methods and equipment previously described were used.[9] Λ_0 was evaluated by the extrapolation methods of Fuoss [10] and Ives *et al.*[11] Results are given in Tables 4 and 5 (concn. in moles l.$^{-1}$; Λ in mho cm.^{2}).

TABLE 5.

2-Hydroxy-3-nitrobenzoic acid (3-nitrosalicylic acid)

10^3c	Λ	10^3K
4·299	309·1	13·3
2·729	330·4	13·6
1·035	359·6	13·0
1·649	347·5	13·4
0·9745	361·3	13·5
0·5023	372·8	13·7

$\Lambda_0 = 388{\cdot}6$

2-Hydroxy-6-nitrobenzoic acid (6-nitrosalicylic acid)

3·239	277·0	5·91
2·274	295·9	5·84
1·625	311·6	5·73
1·055	331·1	5·85
0·7769	341·2	5·78
0·3551	355·0	5·75

$\Lambda_0 = 383{\cdot}9$

2-Chloro-6-hydroxybenzoic acid (6-chlorosalicylic acid)

1·069	286·9	$2{\cdot}37_5$
0·7503	305·2	2·36
0·6156	314·5	2·35
0·5867	316·5	2·34
0·5754	317·9	2·34
0·4475	329·1	2·41
0·4443	327·9	2·32
0·2882	344·2	2·41

$\Lambda_0 = 382{\cdot}6$

3-Hydroxy-2-naphthoic acid

0·7873	285·5	$1{\cdot}94_5$
0·7103	291·3	1·96
0·5666	303·0	1·99
0·5194	306·3	$1{\cdot}95_5$
0·3334	324·8	1·98
0·2948	329·7	$(2{\cdot}01_5)$
0·2525	334·6	2·00
0·2037	339·0	$(1{\cdot}88_5)$
0·1437	348·0	$1{\cdot}92_5$

$\Lambda_0 = 373{\cdot}3$

2-Hydroxy-4-nitrobenzoic acid (4-nitrosalicylic acid)

10^3c	Λ	10^3K
2·444	295·9	5·95
1·304	325·4	5·85
1·225	328·9	5·93
1·052	334·6	5·81
0·9168	339·6	5·82
0·7571	346·0	5·83

$\Lambda_0 = 387{\cdot}5$

2-Hydroxy-3:5-dinitrobenzoic acid (3:5-dinitrosalicylic acid)

5·304	366·0	188
3·247	371·6	195
2·199	374·6	203
2·137	374·9	202
1·852	375·6	204
1·613	376·5	212

$\Lambda_0 = 385{\cdot}0$

5-Bromo-2-hydroxybenzoic acid (5-bromosalicylic acid)

1·349	274·6	$2{\cdot}42_5$
1·164	283·4	2·44
0·6974	310·7	$2{\cdot}46_5$
0·6589	312·8	$2{\cdot}43_5$
0·5515	319·8	2·38
0·4938	325·5	2·44
0·4318	331·0	$2{\cdot}45_5$
0·2210	351·6	2·42

$\Lambda_0 = 382{\cdot}4$

3-Methoxy-2-naphthoic acid *

0·06529	291·6	0·178
0·05475	292·3	0·151
0·03877	303·1	0·132

Λ_0 (assumed) = 375

2-Hydroxy-5-nitrobenzoic acid (5-nitrosalicylic acid)

10^3c	Λ	10^3K
3·643	287·2	7·52
3·214	294·0	7·47
2·457	308·5	7·55
2·204	314·5	7·65
1·525	330·1	7·53
1·075	343·5	7·62
0·8160	351·8	7·63

$\Lambda_0 = 388{\cdot}2$

5-Chloro-2-hydroxybenzoic acid (5-chlorosalicylic acid)

1·369	272·4	2·34
1·216	279·4	2·34
1·033	289·4	2·37
0·8781	297·9	$2{\cdot}35_5$
0·7552	305·8	$2{\cdot}36_5$
0·5976	316·7	2·35
0·5872	317·5	2·35
0·5181	323·1	2·36
0·4819	326·2	2·36
0·2972	343·0	$2{\cdot}31_5$

$\Lambda_0 = 383{\cdot}6$

2-Hydroxy-6-methylbenzoic acid (6-methylsalicylic acid)

1·189	174·5	0·475
1·167	175·5	0·473
0·9182	189·7	0·470
0·8523	195·2	0·478
0·7903	200·0	0·478
0·5463	224·0	0·483
0·4139	241·3	0·482
0·2565	269·6	0·479
0·1796	288·4	0·471
0·1145	309·8	0·467

$\Lambda_0 = 373{\cdot}2$

* The values of dissociation constant of this acid were derived from the classical Ostwald expression, and are very approximate in consequence of the extremely sparing solubility of this acid in water.

One of us (L. G. B.) thanks the Governing Body of Chelsea Polytechnic for a Research Assistantship.

CHEMISTRY DEPARTMENT, CHELSEA POLYTECHNIC,
LONDON, S.W.3.

[*Received, January 17th*, 1957.]

[9] Dippy, Hughes, and Laxton, *J.*, 1954, 1470.
[10] Fuoss, *J. Amer. Chem. Soc.*, 1935, **57**, 488.
[11] Ives, *J.*, 1933, 731; Ives and Sames, *J.*, 1943, 511.

462. *Esters containing Phosphorus. Part XIV.* Some* tert.*-Butyl Esters and Their Reactions.*

By H. Goldwhite and B. C. Saunders.

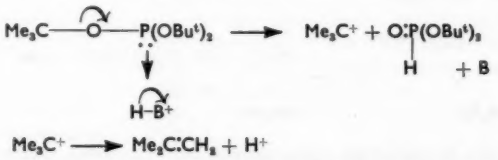
Di-*tert.*-butyl phosphorochloridate reacts in an unusual way with primary aromatic amines, yielding amine salts of mono-*tert.*-butyl *N*-arylphosphoramidates. These salts when heated *in vacuo* give *N*-arylphosphoramidic acids. The complete sequence of reactions constitutes a new method of phosphorylating these amines.

Several workers have prepared *tert.*-butyl esters containing phosphorus. Milobedzki and Sachnowski [1] and Kosolapoff [2] claimed that tri-*tert.*-butyl phosphite was produced by the reaction between 3 mols. of *tert.*-butyl alcohol and 1 mol. of phosphorus trichloride in the presence of a tertiary base, but later Young [3] and Gerrard *et al.*[4] showed that the product was di-*tert.*-butyl phosphite (I). We have confirmed the observations of these later workers and have shown, in addition, that even in the presence of a large excess of tertiary base the product is still the dialkyl phosphite.

In general, excellent yields of primary and secondary trialkyl phosphites are obtained by the reaction between alcohols and phosphorus trichloride in the presence of a tertiary base.[5] In the absence of a tertiary base, the dialkyl hydrogen phosphite is normally produced.[5,6] It is clear therefore that, in these cases, the free acid, not bound as base hydrochloride, is required for dealkylation : [7]

$$(RO)_3P + HCl \longrightarrow Cl^- + (RO)_3PH^+ \longrightarrow RCl + (RO)_2PH(:O)$$

It is necessary to invoke a different mechanism to account for the apparent dealkylation of tri-*tert.*-butyl phosphite (assuming this to be the initial reaction product). In this case, the dealkylation is by a base hydrochloride :



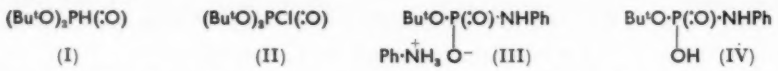
In view of this ease of dealkylation of *tert.*-butyl phosphites under mild conditions and of the known rapid hydrolysis of *tert.*-butyl esters of carboxylic acids,[8,9] it seemed that dealkylation of *tert.*-butyl esters of phosphoramidic acids might be a reasonable method for synthesising the free acids. Accordingly, a series of reactions was designed to effect this.

When di-*tert.*-butyl phosphite was treated with *N*-chlorosuccinimide,[10,11] it yielded di-*tert.*-butyl phosphorochloridate (II) which, being thermally unstable, could not be purified by distillation. The formation, however, of the phosphorochloridate in solution was definitely established by its conversion in high yield into di-*tert.*-butyl phosphoramidate

* Part XIII, *J.*, 1955, 3564.

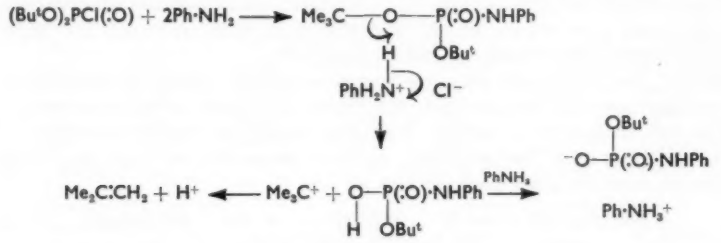
[1] Milobedski and Sachnowski, *Chem. Polski*, 1917, **15**, 34.
[2] Kosolapoff, *J. Amer. Chem. Soc.*, 1952, **74**, 4953.
[3] Young, *ibid.*, 1953, **75**, 4620.
[4] Gerrard, Isaacs, Machell, Smith, and Wyvill, *J.*, 1953, 1920.
[5] McCombie, Saunders, and Stacey, *J.*, 1945, 380.
[6] Cook, Saunders, and Smith, *J.*, 1949, 635.
[7] Gerrard, Nechvatal, and Wilson, *J.*, 1950, 2088.
[8] Skrabal and Jugetz, *Monatsh.*, 1926, **47**, 117.
[9] Skrabal and Zahorka, *ibid.*, 1927, **48**, 459.
[10] Kenner, Todd, and Weymouth, *J.*, 1952, 3675.
[11] Goldwhite and Saunders, *J.*, 1955, 2040.

and di-*tert.*-butyl *N*-benzylphosphoramidate by the action of ammonia and of benzylamine respectively.

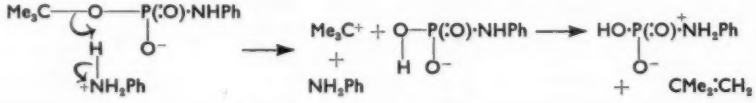


When the phosphorochloridate was allowed to react with aniline, the sole isolable product containing phosphorus was the anilinium salt of mono-*tert.*-butyl *N*-phenylphosphoramidate (III). The structure of (III) was confirmed by analysis, the infrared spectrum, and by conversion into *tert.*-butyl hydrogen *N*-phenylphosphoramidate (IV) on treatment with acids or the hydrogen form of a cation-exchange resin.

The formation of the anilinium salt can be rationalised by assuming that di-*tert.*-butyl *N*-phenylphosphoramidate is first formed and then suffers dealkylation by the aniline hydrochloride produced. The relative stability of the *tert.*-butyl carbonium ion may explain the ease of this dealkylation which occurs under very mild conditions, as shown :



When the anilinium salt was heated *in vacuo* it was converted quantitatively into *N*-phenylphosphoramidic acid. This further dealkylation can be pictured as following a course similar to the first stage :



The identity of the *N*-phenylphosphoramidic acid has been confirmed by analysis, by electrometric titration, and by comparison with the compound prepared by the hydrogenolysis of dibenzyl *N*-phenylphosphoramidate.[12] The acid is formulated as a zwitterion because of its high melting point [13] and the absence of N–H stretching bands in its infrared spectrum.

By similar methods *N*-*p*-chlorophenyl-, *N*-*p*-bromophenyl-, and *N*-*p*-tolyl-phosphoramidic acids have been prepared from the corresponding amines. The *p*-bromophenyl and *p*-tolyl acids have not previously been recorded since the compounds prepared by Otto [14] and Michaelis [15] by hydrolysing *N*-arylphosphoramidic dichlorides have been shown to be *N*-arylphosphorodiamidic acids.[16, 17]

It is interesting that the reaction between di-*tert.*-butyl phosphite, carbon tetrabromide, and benzylamine gave in very good yield a compound identical with di-*tert.*-butyl *N*-benzyl phosphoramidate obtained by the action of the phosphorochloridate on benzylamine. This indirectly confirms Steinberg's suggestion [18] that the first step of this type of reaction

[12] Cook, Ilett, Saunders, Stacey, Watson, Wilding, and Woodcock, *J.*, 1949, 2921.
[13] Clark and Todd, *J.*, 1950, 2030.
[14] Otto, *Ber.*, 1895, **28**, 616.
[15] Michaelis, *Annalen*, 1903, **326**, 129.
[16] Caven, *J.*, 1902, 1367.
[17] Rorig, *J. Amer. Chem. Soc.*, 1949, **71**, 3561.
[18] Steinberg, *J. Org. Chem.*, 1950, **15**, 637.

produces a phosphorohalidate rather than a trihalogenomethylphosphonate. An examination of this particular example using Courtauld space-filling models [19] strongly suggests that di-*tert.*-butyl tribromomethylphosphonate (VI) would be very highly strained, if indeed it could exist at all, whereas di-*tert.*-butyl phosphorobromidate (V) is not strained. The ease of the reaction and the high yield point to the latter (V) as the more likely intermediate.

$$(Bu^tO)_2POH \xrightarrow{CBr_4 + Base} (Bu^tO)_2P(:O)\cdot Br \longrightarrow (Bu^tO)_2P(:O)\cdot NH\cdot CH_2Ph$$

(V)

$(Bu^tO)_2P(:O)\cdot CBr_3$ (VI)

Experimental

Di-tert.-*butyl Phosphite*.—Phosphorus trichloride (45·75 g., 0·33 mole) in ether (60 ml.) was dropped during 2 hr. into a well-stirred solution of *tert.*-butyl alcohol (74 g., 1 mole) and pyridine (1 mole) in ether (400 ml.) cooled in ice–salt. The mixture was stirred for 1 hr. after the addition and then filtered. The filtrate was warmed under reduced pressure to remove low-boiling liquids, and the residue was distilled rapidly to yield di-*tert.*-butyl phosphite, b. p. 66—68°/0·5 mm. (50 g., 77%) (Found: C, 49·6; H, 9·6; P, 15·7. Calc. for $C_8H_{19}O_3P$: C, 49·5; H, 9·8; P, 16·0%). The principal absorption bands * in the infrared spectrum occur at 2976 (aliphatic C–H); 2410 (P–H); 1479, 1395, and 1370 (–CMe_3); 1263 (P=O); 1172, 1071, 1042, 967 (P–O–C); 920, 825, and 700 cm.$^{-1}$.

Reaction between tert.-*Butyl Alcohol and Phosphorus Trichloride in the Presence of a Large Excess of Pyridine*.—Phosphorus trichloride (22·9 g., 0·167 mole) and pyridine (39·5 g., 0·5 mole) in ether (60 ml.) were dropped during 2 hr. into a well-stirred solution of *tert.*-butyl alcohol (37 g., 0·5 mole) and pyridine (0·5 mole) in ether (400 ml.) cooled in ice–salt. The mixture was stirred for 1 hr. after the addition and then filtered. Ether was evaporated from the filtrate by warming under reduced pressure. The infrared spectrum of the undistilled residue contained no absorption bands which were not attributable either to di-*tert.*-butyl phosphite or to pyridine. When the liquid was distilled it gave pyridine and then pure di-*tert.*-butyl phosphite, b. p. 72—74°/1 mm.

Di-tert.-*butyl Phosphorochloridate*.—*N*-Chlorosuccinimide (6·67 g., 0·05 mole) was added in portions to a solution of di-*tert.*-butyl phosphite (9·7 g., 0·05 mole) in carbon tetrachloride (50 ml.) at *ca.* 65°. The mixture was cooled and filtered and the solvent was removed by warming under reduced pressure. The residual liquid decomposed on attempted distillation, but before distillation was a reasonably pure sample of *di*-tert.-*butyl phosphorochloridate* (Found: Cl, 15·3. $C_8H_{18}O_3ClP$ requires Cl, 15·5%).

Di-tert.-*butyl Phosphoramidate*.—A solution of di-*tert.*-butyl phosphorochloridate (0·0215 mole) in ether (30 ml.) was saturated with ammonia. The mixture was filtered and the filtrate evaporated to a crystalline residue, which recrystallised from light petroleum (b. p. 40—60°) as needles of *di*-tert.-*butyl phosphoramidate* sintering at 75—90°, m. p. 122—125° (decomp.) (4·1 g., 91%) (Found: C, 45·8; H, 9·1; N, 7·1. $C_8H_{20}O_3NP$ requires C, 45·9; H, 9·5; N, 6·7%).

Di-tert.-*butyl* N-*Benzylphosphoramidate*.—(1) Benzylamine (4·28 g., 0·04 mole) was slowly added to a cooled solution of di-*tert.*-butyl phosphorochloridate (0·02 mol.) in ether (20 ml.). After 1 hr. the mixture was shaken with water (100 ml.) and ether (50 ml.), and the ethereal layer was separated and dried ($MgSO_4$). On evaporation the residue crystallised, and was twice recrystallised from aqueous ethanol, giving needles of *di*-tert.-*butyl* N-*benzylphosphoramidate*, m. p. 97—98° (5·1 g., 85%) (Found: C, 59·9; H, 8·95; N, 4·7. $C_{15}H_{26}O_3NP$ requires C, 60·2; H, 8·7; N, 4·7%).

(2) *Synthesis using carbon tetrabromide*. Carbon tetrabromide (8·3 g., 0·025 mole) and benzylamine (10·7 g., 0·1 mole) were added to di-*tert.*-butyl phosphite (9·7 g., 0·05 mole) in ether (60 ml.). After a few minutes the mixture became warm and a precipitate separated, and after 4 hr. at room temperature the whole was shaken with ether (40 ml.) and water (100 ml.). The aqueous layer was discarded and the ethereal layer washed with 3N-hydrochloric acid

* The infrared spectra of other phosphorus compounds recorded in this paper were determined and the results confirmed chemical conclusions.

[19] Hartley and Robinson, *Trans. Faraday Soc.*, 1952, **48**, 847.

(3 × 50 ml.) and water (50 ml.) and dried ($MgSO_4$). The ether was evaporated and the residue recrystallised from aqueous methanol as needles (9·3 g., 62%) of di-*tert.*-butyl *N*-benzylphosphoramidate, m. p. 96—98°, alone and mixed with sample prepared as in (1).

Anilinium tert.-*Butyl* N-*Phenylphosphoramidate*.—(1) Di-*tert.*-butyl phosphorochloridate (0·01 mol.) was added to aniline (2·8 g., 0·03 mole). After 2 hr. the solid mass was extracted with boiling benzene (50 ml.) and filtered. The filtrate deposited needles which recrystallised from *cyclo*hexane–ethanol to yield *anilinium* tert.-*butyl* N-*phenylphosphoramidate*, m. p. 140—141° with effervescence followed by resolidification and remelting at 264—270° (decomp.) (Found: C, 59·4; H, 7·8; N, 8·8; P, 9·6. $C_{16}H_{29}O_3N_2P$ requires C, 59·6; H, 7·2; N, 8·7; P, 9·6%).

(2) *Synthesis using carbon tetrabromide*. Carbon tetrabromide (3·32 g., 0·01 mole) and aniline (3·72 g., 0·04 mole) were added to di-*tert.*-butyl phosphite (3·88 g., 0·02 mol.) in ether (40 ml.). The solution became bright orange and the precipitate of aniline hydrobromide that was slowly formed was filtered off. The filtrate was washed with water (4 × 50 ml.) and dried ($MgSO_4$). After removal of the solvent, the residue was dissolved in hot ethanol (20 ml.) and cooled to 5°. The slightly coloured crystals obtained (1·05 g.) had m. p. 142—145°, resolidified, and remelted at 250—260° (decomp.). The infrared spectrum was identical with that of the anilinium *tert.*-butyl *N*-phenylphosphoramidate obtained by method (1).

tert.-*Butyl Hydrogen* N-*Phenylphosphoramidate*.—The anilinium salt (0·2 g., 0·62 mmole) was dissolved in a minimum of water (*ca.* 40 ml.), and concentrated hydrochloric acid (4 ml.) was added. Colourless needles separated and were rapidly filtered off and proved to be tert.-*butyl hydrogen* N-*phenylphosphoramidate* (0·083 g., 58%) which blackened at 240° and had m. p. 253—256° (decomp.) (Found: C, 51·9; H, 7·2; N, 6·3%; Equiv., by electrometric titration, 225 ± 10. $C_{10}H_{16}O_3NP$ requires C, 52·3; H, 7·0; N, 6·1%; Equiv., 229).

The compound prepared by passing a solution of the anilinium salt through a Dowex-50 cation-exchange resin in the hydrogen form was identical with that produced by this acid treatment.

N-*Phenylphosphoramidic Acid*.—Anilinium *tert.*-butyl *N*-phenylphosphoramidate (2·4 g., 7·5 mmoles) was maintained at 80°/0·5 mm. for 18 hr. The product was N-*phenylphosphoramidic acid*, m. p. 267—271° (decomp.) (1·29 g., quantitative) (Found: C, 41·2; H, 4·7; N, 8·3%; Equiv., 85 ± 5, 170 ± 10. Calc. for $C_6H_8O_3NP$: C, 41·6; H, 4·6; N, 8·1%; Equiv., 86·5, 173). A sample prepared by the method of Saunders *et al.*[13] was identical with this compound.

By similar methods the following compounds were prepared: p-*Toluidinium* tert.-*butyl* N-p-*tolylphosphoramidate*, recrystallised from *cyclo*hexane–ethanol as colourless needles, m. p. with bubbling, 147—150°, resetting, and remelting at 250—254° (decomp.) (Found: C, 61·6; H, 7·6; N, 8·2. $C_{18}H_{27}O_3N_2P$ requires C, 61·8; H, 7·7; N, 8·0%).

N-p-*Tolylphosphoramidic acid*, prepared by heating the salt at 80°/0·5 mm. for 20 hr.; m. p. 270—272° (decomp.) (Found: C, 45·0; H, 5·3; N, 7·6%; Equiv., 96 ± 5, 190 ± 10. $C_7H_{10}O_3NP$ requires C, 45·0; H, 5·3; N, 7·5%; Equiv., 93·5, 187).

p-*Chloroanilinium* tert.-*butyl* N-p-*chlorophenylphosphoramidate* recrystallised from *cyclo*hexane as cubes softening at 150°, resetting, and remelting at 250—255° (decomp.) (Found: C, 49·1; H, 5·7; N, 7·4. $C_{16}H_{21}O_3N_2Cl_2P$ requires C, 49·1; H, 5·4; N, 7·2%).

N-p-Chlorophenylphosphoramidic acid, prepared by heating the salt at 80°/1 mm. for 24 hr., blackens at 250° and decomposes at 268—270° (this compound is recorded [20] as blackening at 260° and decomposing at 290°) (Found: C, 34·3; H, 3·7; N, 6·4%; Equiv., 106 ± 5, 212 ± 10. Calc. for $C_6H_7O_3NClP$: C, 34·7; H, 3·4; N, 6·7%; Equiv., 104, 208).

p-*Bromoanilinium* tert.-*butyl* N-p-*bromophenylphosphoramidate* recrystallised from chloroform as needles sintering at 150°, m. p. 260° (decomp.) (Found: C, 40·0; H, 4·7; N, 5·9. $C_{16}H_{21}O_3N_2Br_2P$ requires C, 40·0; H, 4·4; N, 5·8%).

N-p-*Bromophenylphosphoramidic acid*, prepared by heating the salt at 80°/1 mm. for 14 hr., blackens at 255°, melts at 272—274° (decomp.) (Found: C, 28·3; H, 2·8; N, 5·5%; Equiv., 123 ± 5, 250 ± 10. $C_6H_7O_3NBrP$ requires C, 28·5; H, 2·8; N, 5·5%; Equiv., 126, 252).

We are indebted to the D.S.I.R. for a maintenance grant (to H. G.).

UNIVERSITY CHEMICAL LABORATORY, CAMBRIDGE. [*Received, January 28th*, 1957.]

[20] Si-Oh Li, *Acta Chem. Scand.*, 1950, **4**, 610.

XUM

463. *Esters containing Phosphorus. Part XV.* Preparation and Reactions of Diphenylphosphine Oxide.*

By B. B. Hunt and B. C. Saunders.

Williams and Hamilton prepared di-*n*-alkylphosphine oxides, but were unable to isolate any diarylphosphine oxides (*e.g.*, diphenylphosphine oxide).[1] We have succeeded in preparing diphenylphosphine oxide (I) by the action of phenylmagnesium bromide on diethyl hydrogen phosphite:

$$(EtO)_2PH(:O) \longrightarrow Ph_2P(:O)\cdot MgBr \longrightarrow Ph_2PH(:O) \quad (I)$$

We have shown that diphenylphosphine oxide is in equilibrium with diphenylphosphinous acid (II). Infrared measurements indicate that under normal conditions the phosphine oxide form (I) preponderates. However the aqueous solution reacts quantitatively with silver nitrate solution to give silver diphenylphosphinite: this reaction is not instantaneous. Diphenylphosphine oxide was oxidised quantitatively in aqueous solution by bromine yielding diphenylphosphinic acid (III), also produced by dilute hydrogen peroxide solution or acidified potassium permanganate solution.

$$\underset{(I)}{Ph_2PH(:O)} \longrightarrow \underset{(IV)}{Ph_2PCl(:O)} \longrightarrow \underset{(V)}{Ph_2P(:O)\cdot NHPh} \qquad \underset{(III)}{Ph_2P(:O)\cdot OH} \longleftarrow \underset{(II)}{Ph_2P\cdot OH} \longrightarrow Ph_2P\cdot OAg$$

Thionyl chloride converted diphenylphosphine oxide into diphenylphosphinic chloride (IV), the constitution of which was confirmed by an alternative synthesis from the phosphine oxide and *N*-chlorosuccinimide. In these reactions the phosphine oxide almost certainly reacts in the tautomeric form (I). Diphenylphosphinic chloride was readily characterised by its conversion with aniline into the crystalline *NPP*-triphenylphosphinamide (V).

Experimental.—Diphenylphosphine oxide. Bromobenzene (68·4 g.) in ether (100 ml.) was added slowly with stirring to magnesium turnings (12 g.) and ether (100 ml.), and heated under reflux for 15 min. To the cooled reagent, diethyl hydrogen phosphite (20 g.) in ether (80 ml.) was added slowly, with stirring, and the whole heated under reflux for 15 min. (An atmosphere of nitrogen did not increase the yield appreciably.) The mixture was cooled to 0°, 10% hydrochloric acid (200 ml.) was run in slowly and then water (200 ml.). The ether layer was extracted with 2% hydrochloric acid (100 ml. portions) to remove diphenylphosphine oxide. This was ascertained by adding bromine water to a test-sample of the aqueous layer, any diphenylphosphine oxide being converted into insoluble diphenylphosphinic acid. The combined aqueous layers (2·4 l.) were extracted with benzene (50 ml. portions) until the aqueous layer no longer contained diphenylphosphine oxide (bromine-water test). The benzene extracts (650 ml.) were dried (Na_2SO_4) and evaporated, giving *diphenylphosphine oxide* (19·2 g., 66%). The crude product was dissolved in dry ether at 18° and cooled to −60°, yielding colourless hygroscopic needles of the oxide, m. p. 53—56° (14 g., 48%) [Found: C, 71·35; H, 5·4; P, 15·5%; *M* (Rast), 213. $C_{12}H_{11}OP$ requires C, 71·25; H, 5·5; P, 15·3%; *M*, 202].

Principal infrared absorption peaks: 3450, 3050, 2320, 1587, 1484, 1439, 1185, 1162, 1120, 1072, 1027, 1000, 955, 922, 757, 740, 720, 693 cm.$^{-1}$.

Oxidation of diphenylphosphine oxide. (*a*) Quantitatively by bromine. Bromine water (20 ml.; 0·1376N) was added to an aqueous solution of diphenylphosphine oxide (20 ml. containing 0·1457 g.). A precipitate of diphenylphosphinic acid, m. p. 193—195°, appeared immediately (Kosolapoff [2] gave m. p. 190—192°). The excess of bromine was determined by addition of potassium iodide solution and titration with sodium thiosulphate solution [Found: 0·1457 g. of diphenylphosphine oxide required 0·1130 g. of bromine. So 202·2 g. (1 mole) of diphenylphosphine oxide required 15·70 g. of oxygen for oxidation to diphenylphosphinic acid].

* Part XIV, preceding paper.

[1] Williams and Hamilton, *J. Amer. Chem. Soc.*, 1952, **74**, 5418.
[2] Kosolapoff, *ibid.*, 1942, **64**, 2982.

XUM

(*b*) By hydrogen peroxide. Hydrogen peroxide (50 ml.; 20-vol.) was added to diphenylphosphine oxide (2 g.) in water (100 ml.). Diphenylphosphinic acid (m. p. 193—194°) was precipitated within 10 min. at room temperature.

Silver diphenylphosphinite. Diphenylphosphine oxide (0·1406 g.) in water (20 ml.) was added to a known excess of silver nitrate solution (20 ml.; 0·1009N). A precipitate appeared after 5—10 min. at 17° and the reaction required 3—4 hr. for completion. At 100° the reaction time was of the order of 15 min. The silver salt was filtered off (as its solubility product was unknown) and the excess of silver nitrate was determined by Volhard's method [Found: 0·1406 g. of diphenylphosphine oxide required 0·1184 g. of silver nitrate. So 202·2 g. (1 mole) of diphenylphosphine oxide required 170·3 g. of silver nitrate (*M*, 170·0)].

Reaction between diphenylphosphine oxide and thionyl chloride. To diphenylphosphine oxide (9·3 g.) in dry chloroform (50 ml.) was added thionyl chloride (30 g.) in dry chloroform (90 ml.) with stirring in an atmosphere of nitrogen. The mixture was heated for 22 hr. After removal of the chloroform the residue was twice distilled, to give diphenylphosphinic chloride, b. p. 190—194/1 mm. (3·4 g., 32%) (Found: C, 60·8; H, 4·7. Calc. for $C_{12}H_{10}OClP$: C, 60·9; H, 4·3%).

NPP-*Triphenylphosphinamide.* Aniline (1·68 g.) was added to diphenylphosphinic chloride (2·11 g.), the mixture was kept for 1 hr., then extracted with boiling benzene. The benzene was evaporated and the NPP-*triphenylphosphinamide* recrystallised from alcohol as colourless needles, m. p. 242—244° (Found: C, 74·0; H, 5·6; N, 4·8. $C_{18}H_{16}ONP$ requires C, 73·7; H, 5·5; N, 4·8%). Morrison [3] gave m. p. 231—233° for (probably very impure) "diphenylphosphinic anilide," prepared by a different method.

Reaction between diphenylphosphine oxide and N-chlorosuccinimide. *N*-Chlorosuccinimide (2·7 g.) was added slowly to diphenylphosphine oxide (4 g.) in dry chloroform (50 ml.) at 0° with shaking. The solution was then cooled to −5° and succinimide was filtered off, the chloroform removed, and the residue fractionated, giving diphenylphosphinic chloride, b. p. 186—189°/0·9 mm. (1·3 g., 28%) (Found: C, 60·9; H, 4·5. Calc. for $C_{12}H_{10}OClP$: C, 60·9; H, 4·3%). The phosphinic chloride was characterised as *NPP*-triphenylphosphinamide (see above) which, recrystallised from alcohol, had m. p. 242—244°.

We are indebted to the Salters' Institute of Industrial Chemistry for a scholarship (to B. B. H.).

UNIVERSITY CHEMICAL LABORATORY, CAMBRIDGE. [*Received, January 28th*, 1957.]

[3] Morrison, *J. Amer. Chem. Soc.*, 1951, **73**, 5896.

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464. *Replacement of the Hydrazino-group in Substituted Nitrophenylhydrazines by Bromine or Iodine.*

By SHIAM SUNDER JOSHI and DALEEP SINGH DEORHA.

THE compounds tabulated have been prepared by the action of bromine in acetic acid or iodine in alcohol on substituted nitrophenylhydrazines:

Phenylhydrazine used	Benzene formed	Yield (%)	M. p.	Total halogen found (%)	Total halogen reqd. (%)
2-Chloro-4 : 6-dinitro-	2-Chloro-1-iodo-4 : 6-dinitro-	64	119°	49·1	49·5
2-Bromo-4 : 6-dinitro-	2-Bromo-1-iodo-4 : 6-dinitro-	62	116	55·3	55·5
3-Methyl-4 : 6-dinitro-	1-Iodo-3-methyl-4 : 6-dinitro-	65	110	41·5	41·2
3-Methyl-2 : 4 : 6-trinitro-	1-Iodo-3-methyl-2 : 4 : 6-trinitro-	63	146	36·1	36·0
6-Chloro-3-methyl-2 : 4-dinitro-	6-Chloro-1-iodo-3-methyl-2 : 4-dinitro-	62	136	47·6	47·4
4-Chloro-2 : 6-dinitro-	4-Chloro-1-iodo-2 : 6-dinitro-	55	129	49·8	49·5
4-Bromo-2 : 6-dinitro-	4-Bromo-1-iodo-2 : 6-dinitro-	54	125	55·9	55·5
3-Chloro-4 : 6-dinitro-	3-Chloro-1-iodo-4 : 6-dinitro-	62	102	49·8	49·5
2-Chloro-4 : 6-dinitro-	1-Bromo-2-chloro-4 : 6-dinitro-	68	62	41·2	41·0
4-Chloro-2 : 6-dinitro-	1-Bromo-4-chloro-2 : 6-dinitro-	60	106	40·85	41·0

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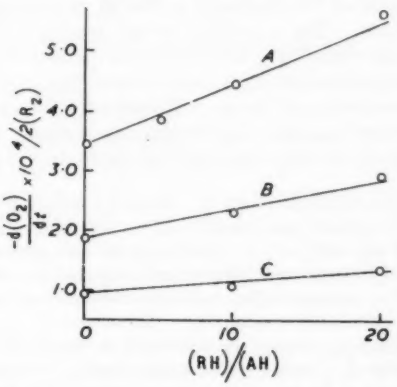
465. *Alkylperoxy-radicals. Part IV.* The First Step in the Reaction with Alkylphenols.*

By A. F. Bickel and E. C. Kooyman.

In previous papers of this series, arguments were given supporting the view that the primary step in the interaction of hindered phenols and alkylperoxy-radicals consists in the removal of hydrogen from the hydroxyl group. Thus, nearly identical antioxidant efficiencies were recorded for 2 : 6-di-*tert.*-butyl-4-methylphenol and 2 : 4 : 6-tri-*tert.*-butylphenol,[1] both yielding analogous reaction products, *viz.*, *cyclo*hexadienones carrying a RO·O group in the 4-position.

On the other hand Hammond *et al.*[2] advocated the reversible addition of RO·O· radicals to the phenolic or amine type of antioxidant, to yield a complex which is then destroyed in an irreversible reaction with a second alkylperoxy-radical. Their principal argument is the finding of almost identical rates of oxidation when *N*-methylaniline (or diphenylamine)



Autoxidation of 9 : 10-*dihydroanthracene retarded by* 2 : 6-*di*-tert.-*butyl*-4-*methylphenol.*

A, 64·84°; *B*, 59·94°; *C*, 54·96°.

and the *N*-deuteroamine are compared as retarders for the autoxidation of tetralin initiated by αα″-azo*iso*butyronitrile. In their opinion, the absence of an isotope effect precludes the primary abstraction of hydrogen from the amino-group.

Generally, a low value for the activation energy of a reaction results in a small isotope effect.[3]

Hence it is obvious that the general argument employed by Hammond *et al.* is inconclusive as long as the activation energy involved is unknown, since it may well be very low. To settle this point for the case of a phenolic antioxidant, we have investigated the autoxidation of 9 : 10-dihydroanthracene (RH) initiated by 2 : 2 : 3 : 3-tetraphenylbutane (R_2) and retarded by various amounts of 2 : 6-di-*tert.*-butyl-4-methylphenol (AH) at three temperatures. The rate of oxidation can be represented (Part II) by :

$$-d(O_2)/dt - 2k_D(R_2) = 2k_D(R_2)k_r(RH)/2k_a(AH)$$

where k_D is the rate constant for dissociation of R_2, k_r is the rate constant for RO·O· + RH ⟶ RO·OH + R· (E_r), and k_a is the rate constant for RO·O· + AH ⟶ RO·OH + A· (E_a). The results are presented in the Figure [$d(O_2)/dt$ is in moles/sec. and the other reactants are in moles]. The activation energy (E_D) for the dissociation of R_2 was

* Part III, *J.*, 1957, 2217.

[1] Bickel and Kooyman, *J.*, 1956, 2215.
[2] Hammond, Boozer, Hamilton, and Sen, *J. Amer. Chem. Soc.*, 1955, **77**, 3238.
[3] Wiberg, *Chem. Rev.*, 1955, **55**, 713.

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calculated from the points on the vertical axis [(RH) = 0; AH in excess]. It was found to be 28·4 ± 0·5 kcal./mole; the value recorded by Ziegler [4] is 30·0 kcal./mole.

The overall temperature coefficient $E = E_D + E_r - E_a$ was calculated from the slopes of the lines in the Figure to be 36·2 ± 0·5 kcal./mole. Hence $E_r - E_a = 7{\cdot}8 \pm 1{\cdot}0$ kcal./mole. From the work of Bolland and collaborators [5] it is known that E_r for various alkenylaromatic compounds varies from 5 to 9 kcal./mole ($Ph{\cdot}CH_2{\cdot}CH{:}CH_2$ 9·2; $Ph{\cdot}CH_2{\cdot}CH{:}CMe_2$ 5·3); for 9 : 10-dihydroanthracene we may assume this value to be about 7 kcal./mole. It follows that E_a will be close to zero, which, in turn, will lead to a very small isotope effect. In our opinion, therefore, the absence of isotope effects cannot be taken as evidence against removal of hydrogen from the hydroxyl group of phenols as the primary step.

The above reasoning implies that the reaction of a phenol with a less active attacking radical might provide an opportunity of detecting isotope effects, since the activation energy would be higher. In order to investigate this possibility, diphenylpicrylhydrazyl radicals have been allowed to react with a large excess of 2 : 6-di-*tert.*-butyl-4-methylphenol in toluene at 20° and 30° and also with the deuterated analogue. The rate of removal of the hydrazyl is strictly of first order with respect to hydrazyl up to high conversions. The activation energy, calculated from the bimolecular rate constants (k_{bi}) at 20° and 30°, was 5·3 ± 0·5 kcal./mole, whilst the isotope effect at 20° showed a value of 1·95. This provides strong evidence that in this case the rate-determining step consists in an attack at the hydroxyl group. Admittedly, in view of the difference between diphenylpicrylhydrazyl radicals and alkylperoxy-radicals, the above result does not definitely prove that the latter radicals also react at the hydroxyl group.

Experimental (with W. Roest).—*Starting materials.* Deuteration of 2 : 6-di-*tert.*-butyl-4-methylphenol was carried out by refluxing a solution in benzene with changes of 99·9% D_2O until 85—86% of the OD-compound was present, as determined by infrared spectroscopy.

Diphenylpicrylhydrazyl was prepared according to Goldschmidt and Reun's directions.[6]

The other starting materials were prepared as described in Parts I and II.

Initial rates of oxidation. These were determined as recorded in Part II.

Rates of removal of diphenylpicrylhydrazyl. These were measured spectrophotometrically at 6000 Å. In a typical experiment a two-compartment flask was supplied with 3 ml. of a solution of 21 mg. of 2 : 6-di-*tert.*-butyl-4-methylphenol in toluene and with 10 ml. of a solution containing 1·96 mg. of diphenylpicrylhydrazyl in toluene. The flask was placed in a thermostat at 20° and at zero time the solutions were mixed and the recording Cary spectrophotometer set in motion. Immediately afterwards the solution was transferred to the cell of the instrument and the extinction at 6000 Å was measured continuously.

Temp.	20·0°	20·0°	30·0°
Phenol (10^{-3} mole/l.)	7·37 *	7·35	7·35
Hydrazyl (10^{-3} mole/l.)	0·392	0·385	0·385
k_{bi} (l. mole^{-1} sec.$^{-1}$)	0·046 †	0·078	0·105

* 85% deuterated. † Recalc. for pure D compound = 0·040.

The authors thank the Management of the Koninklijke/Shell-Laboratorium, Amsterdam, for their permission to publish this Note.

Koninklijke/Shell-Laboratorium, Amsterdam. [*Received, September 19th,* 1956.]

[4] Ziegler, *Annalen*, 1942, **551**, 150.
[5] Bolland, *Quart. Rev.*, 1949, **3**, 1.
[6] Goldschmidt and Reun, *Ber.*, 1922, **55**, 628.

466. *A Determination of the Heat of Formation of Potassium Manganate.*

By R. A. W. Hill and (the late) J. F. Williamson.

During recent investigations of combustion in solid mixtures of potassium permanganate and metals [1] it was necessary to calculate heats of plausible reactions for comparison with observed heats. For this the heat of formation of potassium manganate, a possible reduction product of potassium permanganate, was needed.

Potassium manganate cannot conveniently be prepared as a pure crystalline substance because of its instability,[2] but the ice-cold, alkaline, aqueous solution is stable for long periods. Thus the heat of formation in solution can be determined by measuring the heat of reduction of potassium permanganate under these conditions. Reduction with hydrogen peroxide may be represented by the three equations :

$$(1)\quad 2KMnO_4 + H_2O_2 + 2KOH \longrightarrow 2K_2MnO_4 + 2H_2O + O_2 + Q_1$$

$$(2)\quad K_2MnO_4 + H_2O_2 \longrightarrow \tfrac{1}{2}K_2O,2MnO_2\downarrow + \tfrac{1}{2}H_2O + KOH + O_2 + Q_2$$

$$(3)\quad H_2O_2 \xrightarrow{K_2O,2MnO_2} H_2O + \tfrac{1}{2}O_2 + Q_3$$

Knowledge of Q_1 allows $\Delta H_f K_2MnO_4$(aq.) to be calculated from tabulated heats of formation [3] of potassium permanganate, potassium hydroxide, hydrogen peroxide, and water. Direct measurement of Q_1 is not easy because even with good stirring reactions (1) and (2) are not quite consecutive. This difficulty has been overcome by use of a special method, in which hydrogen peroxide solution is added at a constant rate to potassium permanganate solution. The rate of rise in temperature at any time is then proportional to a weighted mean of the heats of the reactions then occurring.

Experimental.—Potassium permanganate solution (3·5 g. in 500 ml.), approx. 5N in potassium hydroxide, was contained in a Dewar flask surrounded by ice and water; a pipette containing 20-vol. hydrogen peroxide [about 20% more than that required for reactions (1) and (2)] was completely immersed in this solution. The peroxide was blown into the permanganate solution by means of a steady stream of nitrogen, precooled to 0°, and the temperature was recorded. A typical temperature–time curve is shown in the Figure. It is simpler than was expected in that there is no change in slope during reactions (1) and (2). On the other hand the change from reaction (2) to reaction (3) is sharply indicated. We therefore conclude that Q_1 and Q_2 have nearly the same value and that this may be calculated from the temperature rise A—B and the electrical equivalent of the system, giving :

$$Q_1 = \tfrac{1}{3}(Q_1 + 2Q_2) = 35{\cdot}5 \text{ kcal./mole.}$$

Another way is to compare the slopes corresponding to Q_1 and Q_3; then

$$\frac{Q_3}{Q_1} = \frac{(dT/dt)_3}{(dT/dt)_1}$$

where Q_3 is to be calculated from the tabulated heats of formation [3] of hydrogen peroxide and water. This procedure gives $Q_1 = 35{\cdot}7$ kcal./mole, which is in good agreement.

The composition of the precipitated manganite was investigated to check the correctness of equation (2), particular attention being given to the oxygen : manganese ratio, which affects

[1] Hill, *Proc. Roy. Soc.*, 1954, *A*, **226**, 455; Hill and Wallace, *Nature*, 1956, **178**, 692.
[2] Duke, *J. Phys. Chem.*, 1952, **56**, 882.
[3] "Selected Values of Chemical Thermodynamic Properties," Circular 500, Nat. Bur. Stand., U.S.A., 1952.

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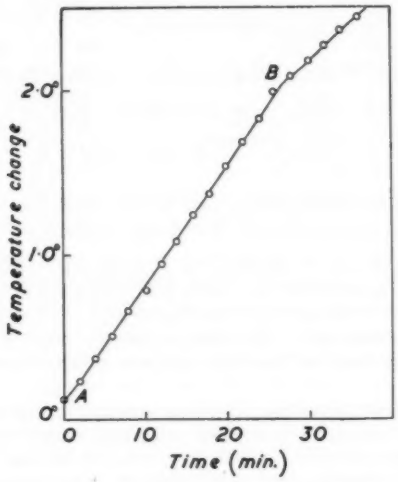
the calculation of Q_1 from $Q_1 + 2Q_2$. The procedure followed was that described by Maxwell, Butler, and Thirsk [4] with the difference that the potassium was estimated by precipitation as cobaltinitrite instead of photometrically. The composition was found to correspond to $1{\cdot}04K_2O,2MnO_{1{\cdot}97}(xH_2O)$, or within the limits of error $K_2O,2MnO_2(xH_2O)$, as required by equation (2). The water content could not be determined because washing and drying the precipitate altered the Mn : O and the K : O ratio, but this does not affect the calculation of Q_1.

Two complete runs were carried out, giving four values of Q_1 : by temperature rise *A*—*B*, 35·4, 35·7; by ratio of slopes, 35·4, 36·0 kcal./mole; average 35·6 ± 1·5 kcal./mole. The error was calculated from estimates of the accuracy of measurement of temperature rise *A*—*B* (±2%), of slope (1) (±2%), slope (3) (±4%), of electric power (±1%), and of stoicheiometry, as indicated by the oxygen : manganese ratio of the precipitate. Three successive determinations of an electrical equivalent with different voltages and times of heating gave 668, 671, 669 cal. °c^{-1}, indicating that the random error in this part of the experiment is less than the systematic error (±1%).



The heats of formation of hydrogen peroxide, potassium hydroxide, and water are very well established and do not contribute to the error in the calculated heat of formation of potassium manganate. That of potassium permanganate rests on Thomsen's early work and is less certain; tentatively we allow an extra ½ kcal. for this. Then :

$$Q_1 = 35{\cdot}5 \pm 1{\cdot}5;\ \Delta H_f K_2MnO_4(\text{aq.}) = -273 \pm 2 \text{ kcal./mole.}$$

It will be seen that a bigger uncertainty than 2 kcal. is involved below in allowing for the heat of solution.

Discussion.—For the purpose of calculating heats of solid–solid reactions a heat of solution assumed to be the same as that of $KMnO_4$ (10 kcal./mole) was added to the above value to give :

$$\Delta H_f K_2MnO_4(\text{cryst.}) = -283 \text{ kcal./mole}$$

The difference between this and Mixter's value for crystalline sodium manganate,[3] −274 kcal./mole, obtained by a dry-way method, is typical of corresponding sodium and

[4] Maxwell, Butler, and Thirsk, *J.*, 1952, 4210.

potassium salts, the heats of formation of which usually differ by about 6 kcal./g.-atom of alkali metal. Both values, therefore, are probably correct to within 4 kcal., which is a useful accuracy for present requirements.

The authors thank Dr. A. P. Zeelenberg for analysing the precipitated potassium manganite.

IMPERIAL CHEMICAL INDUSTRIES LIMITED, NOBEL DIVISION,
RESEARCH DEPARTMENT, STEVENSTON, AYRSHIRE. [*Received, November 23rd,* 1956.]

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467. *The Vapour Pressures of Some Solid Organic Compounds.*

By R. LITTLEWOOD.

DURING recent work on the evaporation coefficient,[1] effusion rates through small orifices of the saturated vapours of various solid organic compounds were determined. From these results, the saturation vapour pressures have been calculated according to Knudsen's method.[2]

Experimental.—The apparatus was essentially similar to the second described by Bradley, Evans, and Whytlaw-Gray (ref. 3, p. 387), but the differential method was not employed. The ends of the two small glass effusion tubes were closed by sheet platinum caps fused to the glass and pierced by holes, through which effusion took place. Hole diameters ranged from 1 to 3 mm. The holes were drilled by clamping the platinum sheet between two sheets of ¼ in. brass and using a pillar drill; they were perfectly circular and free from " burrs ". The area of each hole was found, with good agreement in several determinations, by photographing the silhouette with a photomicrographic apparatus and weighing the image of the hole cut from a print on photographic paper. The method was calibrated by use of a ¼ mm. graticule. The hole diameters were checked by means of a travelling microscope, after fusion of the discs into the tubes. Small corrections (about 3%) were applied to the areas to allow for the thickness of the platinum foil.

Crystals of the material to be studied were finely powdered, introduced into the effusion tubes, and then fused and allowed to run over the glass surface so that a solid film of large surface area was formed in the vessel. Several tubes with different hole sizes were used for each substance.

The filled tubes, in pairs, were subjected to high vacuum in the apparatus for about an hour, after which dry air was admitted and the tubes weighed in turn on an analytical microbalance against an empty tube which had been similarly treated. The two tubes were replaced in the apparatus and allowed to come to equilibrium with the thermostat. The apparatus was then evacuated, a technique which ensured that the pressure fell below 10^{-3} mm. within 30 sec. being used. A half-minute was subtracted from the duration of all runs to allow for this. At the end of the run, dry air was admitted to the apparatus and the effusion tubes were removed and weighed as before.

Solid carbon dioxide–acetone was used in the cold traps. Materials were purified by recrystallisation twice from a suitable solvent and the setting points of the purified materials were checked against data from standard references.

Vapour pressures were calculated from $p = qT^{\frac{1}{2}}/(3{\cdot}50AM^{\frac{1}{2}})$, where p = vapour pressure (mm.), q = rate of effusion (g. per min.), T = absolute temperature, M = molecular weight of effusing vapour, and A = area of orifice (cm.^{2}).

Results.—Calibration with benzophenone, recrystallised twice from light petroleum (b. p. 60—80°), gave a vapour pressure of $3{\cdot}14 \times 10^{-4}$ mm. at 20·0° (mean of 4 determinations, mean deviation 7%) (cf. $3{\cdot}24 \times 10^{-4}$ mm. calculated from the data of Neumann and

[1] Littlewood and Rideal, *Trans. Faraday Soc.*, 1956, **52**, 1598.
[2] Knudsen, *Ann. Physik*, 1909, **29**, 179.
[3] Bradley, Evans, and Whytlaw-Gray, *Proc. Roy. Soc.*, 1946, **186**, *A*, 368.

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Völker [4]). The results for each material studied showed a similar scatter (see Table), but there was no apparent dependence on orifice diameter or on the duration of the run. It was inferred that no errors were arising due to self-cooling or to uncertainties in the exact time at which effusion commenced, and that the apparatus was operating satisfactorily.

An Arrhenius plot of the results for lauric acid gave a latent heat of sublimation of 28,000 ± 700 cal./mole.

Material	Temp.	No. of determinations	Mean deviation (%)	Vapour pressure (mm. Hg)	Material	Temp.	No. of determinations	Mean deviation (%)	Vapour pressure (mm. Hg)
Stearic acid	60°	1	—	$1{\cdot}42 \times 10^{-6}$	Myristic acid	40°	2	4	$1{\cdot}10 \times 10^{-5}$
Lauric acid	20	8	4	$4{\cdot}91 \times 10^{-6}$	Hexadecanol	30	2	8	$3{\cdot}06 \times 10^{-6}$
,,	25	2	5	$8{\cdot}80 \times 10^{-6}$	Tetradecanol	20	4	9	$1{\cdot}03 \times 10^{-5}$
,,	30	8	7	$2{\cdot}34 \times 10^{-5}$	Phenanthrene	20	4	3	$5{\cdot}67 \times 10^{-5}$
,,	35	2	8	$4{\cdot}36 \times 10^{-5}$	Diphenylmethanol	20	6	6	$2{\cdot}73 \times 10^{-5}$
,,	40	8	9	$1{\cdot}09 \times 10^{-4}$	Erythritol ...	20	1	—	$<10^{-8}$

KING'S COLLEGE, LONDON, W.C.2. [*Received, November 28th*, 1956.]

[4] Neumann and Völker, *Z. phys. Chem.*, 1932, **161**, 33.

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468. *Some Potentially Cytotoxic Alkyl Sulphonates.*

By W. C. J. Ross and (in part) W. DAVIS.

2-CHLOROETHYL METHANESULPHONATE is known to be effective in preventing the growth of a transplanted rat tumour [1] and to have unusual mutagenic properties.[2] Some related sulphonic esters have now been prepared for biological testing.

The 2-chloroethyl ester may be prepared by heating a mixture of ethylene chlorohydrin and methanesulphonyl chloride until no more hydrogen chloride is evolved [3] but a more general method is to treat the alcohol with the acid chloride in the presence of pyridine at low temperature. Methyl and ethyl butane-1 : 4-disulphonate, however, were more conveniently prepared from the diacid chloride and sodium alkoxide in the corresponding alcohol.

To increase their aqueous solubility, toluene-*p*-sulphonic esters were oxidised to the corresponding *p*-carboxy-derivatives which were administered as sodium salts.

Kiprijanow [4] reported that esters of 2 : 4-dinitrobenzenesulphonic acid are highly reactive as alkylating agents and this has prompted the preparation of the 2-chloroethyl ester. In this instance owing to the greater reactivity of the ester it was necessary to use 2 : 6-lutidine in place of pyridine and to carry out the reaction at −40°.

The effectiveness of the compounds as inhibitors of the transplanted Walker rat carcinoma is shown in the Table. None of the compounds is more effective than the original chloroethyl ester but methyl, ethyl, and fluoroethyl methanesulphonate are of the same order of activity when given at somewhat higher dose levels.

Experimental.—Preparation of alkyl sulphonates: general method. The alcohol (1 mole) in dry pyridine (150 ml.) and ether (150 ml.) at −10° to 0° was stirred whilst methanesulphonyl chloride (1 mole) was added during 1 hr. After being at 0° overnight the mixture was poured on ice–water containing concentrated sulphuric acid (75 ml.). An ether extract was dried (K_2CO_3–Na_2SO_4) and distilled under reduced pressure in the presence of a few pieces of potassium

[1] Haddow and Ross, *Nature*, 1956, **177**, 995.
[2] Fahmy and Fahmy, *ibid.*, p. 996.
[3] Cf. Clemo and Perkin, *J.*, 1922, **121**, 644.
[4] Kiprijanow, XIVth Internat. Cong. Pure Appl. Chem. Handbook, 1955, p. 320.

Compound	B. p./mm.	n_D (temp.)	Formula	Required (%) C	H	Cl	S	Found (%) C	H	Cl	S	Biolog. activity
Methyl methanesulphonate †	96—98°/19 [a]	1·4150 (20°)	—	—	—	—	—	—	—	—	—	+
Ethyl ,, †	90°/10 [b]	1·4194 (15°)	—	—	—	—	—	—	—	—	—	+
n-Propyl ,,	115°/21	1·4209 (20°)	$C_4H_{10}O_3S$	34·8	7·3	—	23·2	34·2	7·2	—	23·2	− ve
n-Butyl ,, †	118°/14 [c]	1·4249 (20°)	$C_5H_{12}O_3S$	39·4	8·0	—	21·1	38·9	8·1	—	21·0	− ve
Methyl ethanesulphonate *†	100—101°/24 [d]	1·4189 (18°)	$C_3H_8O_3S$	29·0	6·5	—	25·8	29·1	6·4	—	25·8	Low
Ethyl ,, *†	108—112°/24 [e]	1·4232 (18°)	$C_4H_{10}O_3S$	34·8	7·3	—	23·2	35·5	7·5	—	23·8	− ve
2-Fluoroethyl methanesulphonate	130°/19	1·4150 (21°)	$C_3H_7O_3FS$	25·3	5·0	—	22·5	25·1	4·8	—	22·7	+
2-Chloroethyl ,,	130°/11 (M. p. 5—6°)	1·4570 (19°)	$C_3H_7O_3ClS$	22·7	4·5	22·4	20·3	23·0	4·6	22·0	20·3	+
2-Bromoethyl ,,	126—128°/5	1·4835 (19°)	$C_3H_7O_3BrS$	17·7	3·5	(Br, 39·3)	—	17·9	3·5	(Br, 38·5)	—	− ve
2-Iodoethyl ,,	140°/6	1·5300 (21°)	$C_3H_7O_3IS$	14·4	2·8	(I, 52·0)	—	14·3	2·9	(I, 51·0)	—	− ve
2-Cyanoethyl ,,	(M. p. 34—36°) [1]	—	$C_4H_7O_3NS$	32·2	4·7	(N, 9·4)	21·5	32·0	4·5	(N, 9·4)	20·7	− ve
2-Chloroethyl toluene-*p*-sulphonate [f]	205—208°/20	1·5303 (18°)	—	—	—	—	—	—	—	—	—	− ve
,, carboxybenzenesulphonate	(M. p. 186—188°) [g]	—	$C_9H_9O_5ClS$	40·8	3·7	13·4	12·1	40·9	3·5	13·4	12·1	− ve
,, ethanesulphonate *	128—130°/13	1·4559 (18°)	$C_4H_9O_3ClS$	27·8	5·3	—	—	28·1	5·2	—	—	+
,, propane-1-sulphonate	146°/16	1·4565 (19°)	$C_5H_{11}O_3ClS$	32·4	6·0	19·1	17·2	32·3	5·9	19·1	16·5	− ve
,, toluene-ω-sulphonate *	(M. p. 47°) [g]	—	$C_9H_{11}O_3ClS$	46·0	4·7	15·1	13·6	45·7	4·6	15·2	13·0	− ve
Ethylene 1 : 2-di-(*p*-carboxybenzenesulphonate)	(M. p. 262—264°) [4]	—	$C_{16}H_{14}O_{10}S_2$	44·7	3·3	—	14·9	44·6	3·5	—	14·4	− ve
1-Chloro-2-methanesulphonyloxypropane [f]	132—133°/15	1·4530 (20°)	$C_4H_9O_3ClS$	27·8	5·3	20·6	18·6	27·7	5·1	20·8	18·2	− ve
3-Chloropropyl methanesulphonate	144—146°/13	1·4588 (16°)	$C_4H_9O_3ClS$	27·8	5·3	20·6	18·6	27·7	4·9	20·6	18·7	Low
1 : 3-Dichloro-2-methanesulphonyloxypropane	160—162°/13	1·4825 (20°)	$C_4H_8O_3Cl_2S$	23·2	3·9	34·3	15·5	23·9	4·1	34·5	14·5	− ve
1 : 3-Dichloro-2-toluene-*p*-sulphonyloxypropane†	229—230°/20 [h]	1·5350 (20°)	$C_{10}H_{12}O_5Cl_2S$	42·4	4·3	25·1	—	42·6	4·2	25·1	—	− ve
1 : 3-Dichloro-2-*p*-carboxybenzenesulphonyloxypropane	(M. p. 206—209°) [5]	—	$C_{10}H_{10}O_5Cl_2S$	38·4	3·2	22·7	—	38·5	3·4	22·9	—	Low
1-Bromo-3-chloro-2-methanesulphonyloxypropane	164—166°/14	1·5002 (19°)	$C_4H_8O_3BrClS$	19·1	3·2	(Total halogen 45·8)	12·8	19·8	3·3	(Total halogen 45·2)	13·0	+
1 : 2-Dibromopropyl methanesulphonate	190—192°/16	1·5292 (16°)	$C_4H_8O_3Br_2S$	16·2	2·7	—	10·8	16·9	2·9	—	11·0	Low
Propylene 1 : 2-dimethanesulphonate	(M. p. 54—56°) [6]	—	$C_5H_{12}O_6S_2$	25·9	5·2	—	27·6	26·0	5·2	—	27·0	− ve
4-Chlorobutyl methanesulphonate	166—170°/15	1·4602 (18°)	$C_5H_{11}O_3ClS$	32·4	6·0	—	—	32·6	6·2	—	—	Low
2-Chloroethyl 2 : 4-dinitrobenzenesulphonate *	(M. p. 106·5°) [7]	—	$C_8H_7O_7N_2ClS$	30·9	2·3	(N, 9·0)	—	31·1	2·4	(N, 8·6)	—	− ve
Dimethyl butane-1 : 4-disulphonate	(M. p. 93—94°) [8]	—	$C_6H_{14}O_6S_2$	29·7	5·7	—	26·3	29·8	5·9	—	26·1	− ve
Diethyl butane-1 : 4-disulphonate	(M. p. 64—65°) [8]	—	$C_8H_{18}O_6S_2$	35·1	6·6	—	23·4	35·2	6·7	—	23·9	− ve

[a] Voss and Blanke (*Annalen*, 1931, **485**, 258) give b. p. 101—102°/25 mm., n_D^{17} 1·4157. [b] Billeter (*Ber.*, 1905, **38**, 2018) gives b. p. 85—86°/10 mm. [c] Sekera and Marvel (*J. Amer. Chem. Soc.*, 1933, **55**, 345) give b. p. 105—106°/6 mm., n_D^{25} 1·4319. [d] Carius (*J. prakt. Chem.*, 1870, **2**, 270) gives b. p. 197·5—200·5°. [e] Meuwsen and Gebhardt (*Ber.*, 1937, **70**, 792) give b. p. 88·5—89°/8—9 mm. [f] Prepared by Clemo and Perkin's method (*J.*, 1922, **121**, 642); they give b. p. 210°/21 mm. and Tipson and Cretcher (*J. Amer. Chem. Soc.*, 1942, **64**, 1162) give n_D^{20} 1·5280. [g] Prepared by the method of Sletzinger, Chamberlin, and Tishler (*ibid.*, 1952, **74**, 5619) who give b. p. 76—77°/0·4 mm. [h] Blanchard (*Bull. Soc. chim. France*, 1927, **41**, 824) gives b. p. 180—210°/13 mm., n_D 1·5357.

* These compounds were prepared by Dr. W. Davis. † These known compounds were prepared by our general method.

[1] Prisms from methanol. [2] Needles from benzene. [3] Prisms from *cyclo*hexane. [4] Prisms from acetone. [5] Plates from benzene. [6] Prisms from acetone–ether. [7] Needles from benzene–*cyclo*hexane. [8] Plates from chloroform–pentane.

carbonate to prevent autocatalytic decomposition.[5] For the more reactive methanesulphonates, *e.g.*, those from methanol and ethanol, it was advisable to keep the temperature below −30° continuously before pouring on ice.

2-Chloroethyl p-*carboxybenzenesulphonate.* 2-Chloroethyl toluene-*p*-sulphonate (3 g.) in concentrated sulphuric acid (30 ml.) and water (30 ml.) was treated slowly on a steam-bath with chromic acid (8 g.) in water (20 ml.). After ½ hr. solid began to separate and after addition of water the mixture was extracted with ether (500 ml.). The acid, which was extracted from the ether layer with 2N-sodium carbonate and recovered by acidification, formed prismatic needles, m. p. 186—188°, from benzene. The oxidation could also be carried out in glacial acetic acid without the addition of sulphuric acid. 1 : 2-Di-*p*-carboxybenzenesulphonyloxyethane and 1 : 3-dichloro-2-*p*-carboxybenzenesulphonyloxypropane were similarly prepared.

2-Chloroethyl 2 : 4-dinitrobenzenesulphonate. 2 : 4-Dinitrobenzenesulphonyl chloride (14 g.) was added during ½ hr. to a stirred solution of ethylene chlorohydrin (50 ml.) in dry 2 : 6-lutidine (50 ml.) and ether (25 ml.) at −40°. After 4 hr. the temperature was allowed to rise to 0° and the mixture was poured on ice–water containing concentrated sulphuric acid (20 ml.). The *ester* which was extracted with chloroform formed yellow needles (9·6 g.), m. p. 104·5—106·5°, from benzene–*cyclo*hexane (1 : 3).

*Esters of butane-*1 : 4-*disulphonic acid.* To a cooled solution of sodium (0·91 g.) in methanol (100 ml.) was added a solution of butane-1 : 4-disulphonyl chloride (5 g.) in methanol (25 ml.). After 1 hour's shaking at room temperature the solvent was removed under reduced pressure. The residue was extracted with chloroform (3 × 25 ml.) and on the addition an excess of pentane the *dimethyl ester* separated as plates. The diethyl ester was similarly prepared.

This investigation was supported by grants to this Institute from the British Empire Cancer Campaign, the Jane Coffin Childs Memorial Fund for Medical Research, the Anna Fuller Fund, and the National Cancer Institute of the National Institutes of Health, U.S. Public Health Service. The authors thank Professor A. Haddow for permission to quote the results of tumour-growth inhibition studies.

CHESTER BEATTY RESEARCH INSTITUTE,
INSTITUTE OF CANCER RESEARCH: ROYAL CANCER HOSPITAL,
FULHAM ROAD, LONDON, S.W.3. [*Received, December 12th,* 1956.]

[5] Cf. Scott and Lutz, *J. Org. Chem.*, 1954, **19**, 830.

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469. *Synthesis of 2 : 3 : 9-Trimethyl- and 2 : 3 : 8 : 9-Tetramethylphenanthrene.*

By W. CARRUTHERS and J. D. GRAY.

THE two compounds named in the title have been synthesised, for comparative purposes, from 2 : 3 : 6-trimethylnaphthalene. Reaction with succinic anhydride in presence of aluminium chloride afforded two homogeneous acids in small yield. One of these exhibited three regions of ultraviolet absorption typical of 2-acylnaphthalenes,[1] and is clearly the 2-substitution product (I). Huang-Minlon reduction of the carbonyl group and cyclisation of the butyryl chloride with stannic chloride gave the tetrahydro-oxophenanthrene (II), and hence, by standard methods, 2 : 3 : 9-trimethylphenanthrene (III). In agreement with its assigned structure the ketone (II), like other 1-acylnaphthalenes,[1] showed only two regions of absorption (max. at 222 and 330—340 mμ).

An attempt to prepare 2 : 3 : 5 : 9-tetramethylphenanthrene from the ketone (II) and methylmagnesium iodide was unsuccessful. Dehydration and dehydrogenation of the crude alcohol by palladium gave only a mixture of phenanthrene derivatives. A similar

[1] Dannenberg and Dannenberg-von Dressler, *Annalen*, 1955, **593**, 246.

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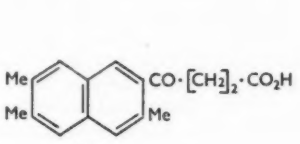
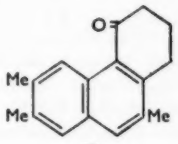
difficulty was encountered by Bendas and Djerassi [2] in an attempt to prepare 4-ethylphenanthrene, and is presumably due to migration and elimination of the alkyl group from the sterically hindered 4-position during dehydrogenation.[3]

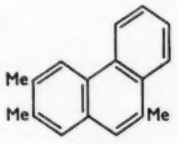
The second acid isolated from the Friedel–Crafts reaction must be a 1-naphthoylpropionic acid, and, in agreement, the ultraviolet absorption spectrum was similar to that of other 1-acylnaphthalenes.[1] Reduction and cyclisation (at 0°), as above, gave the



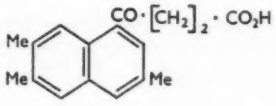
(I)



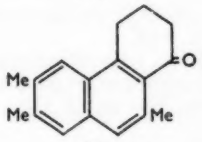
(II)



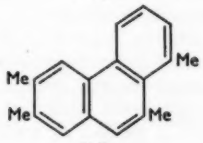
(III)



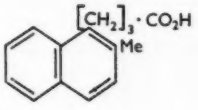
(IV)



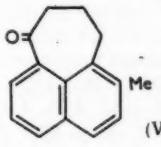
(V)



(VI)



(VII)



(VIII)

ketone (V) in high yield, having a typical 2-acylnaphthalene spectrum. Reaction of the ketone with methylmagnesium iodide, dehydration, and dehydrogenation gave 2 : 3 : 8 : 9-tetramethylphenanthrene (VI) with characteristic phenanthrene absorption. Production of a phenanthrene derivative by this series of reactions confirms the structure assigned to the ketone (V). The structure of the keto-acid produced is thus established as (IV) : cyclisation of the butyric acids derived from the three other possible keto-acids would not have produced a tetrahydro-oxophenanthrene unless accompanied by methyl migration and this seems unlikely under the conditions used. This is supported by the fact that cyclisation of γ-(2-methyl-1-naphthyl)butyryl chloride (VII) with stannic chloride at 45° is reported [4] to yield the ketone (VIII).

Experimental.—Ultraviolet absorption spectra were determined in 95% ethanol with a Unicam spectrophotometer.

Reaction of 2 : 3 : 6-trimethylnaphthalene with succinic anhydride. 2 : 3 : 6-Trimethylnaphthalene (10 g.) and succinic anhydride (5·9 g.) were added to an ice-cold solution of aluminium chloride (15·3 g.) in nitrobenzene (60 c.c.), then kept at room temperature for 3 hr. Ice and hydrochloric acid were added, and nitrobenzene was removed with steam. The residue was extracted with ether, and the extract shaken with aqueous sodium carbonate. Acidification and crystallisation from methanol gave β-(3 : 6 : 7-*trimethyl*-1-*naphthoyl*)*propionic acid* (IV) (1·3 g.), m. p. 183—188° (Found : C, 75·8; H, 6·8. $C_{17}H_{18}O_3$ requires C, 75·5; H, 6·7%). Light absorption : max. 220—225 (infl. 250—255), 300—330 mμ [log ε 5·0 (4·42), 3·96]. The *methyl ester* had m. p. 86° (Found : C, 75·8; H, 7·3. $C_{18}H_{20}O_3$ requires C, 76·05; H, 7·1%).

The crude residual mixture of acids was esterified with diazomethane, and the esters crystallised from methanol. *Methyl* β-(3 : 6 : 7-*trimethyl*-2-*naphthoyl*)*propionate* (1·3 g.) had m. p.

[2] Bendas and Djerassi, *J. Amer. Chem. Soc.*, 1956, **78**, 2474.
[3] Haworth, Mavin, and Sheldrick, *J.*, 1934, 454.
[4] Cagnaint and Cagnaint, *Bull. Soc. chim. France*, 1952, 970.

93—94° (Found : C, 75·7; H, 7·0%) and gave, on hydrolysis, the *acid*, needles (from methanol), m. p. 165—172° (Found : C, 75·4; H, 6·6%). Light absorption : max. 255, 290, 340 mμ (log ε 4·75, 4·04, 3·17).

γ-(3 : 6 : 7-*Trimethyl*-2-*naphthyl*)*butyric acid*. Methyl β-(3 : 6 : 7-trimethyl-2-naphthoyl)propionate (1 g.), sodium hydroxide (0·5 g.), and 90% hydrazine hydrate (0·5 c.c.) in diethylene glycol (8 c.c.) were boiled for 1 hr. The temperature was raised to 195—200° by distilling off water, and refluxing continued for 3 hr. The solution was diluted with water and acidified, and the product extracted with ethyl acetate. The *acid*, crystallised from benzene–light petroleum (b. p. 40—60°), had m. p. 164° (Found : C, 79·5; H, 7·5. $C_{17}H_{20}O_2$ requires C, 79·65; H, 7·9%).

1 : 2 : 3 : 4-*Tetrahydro*-6 : 7 : 10-*trimethyl*-4-*oxophenanthrene*. Phosphorus pentachloride (0·4 g.) and the above butyric acid (0·4 g.) in benzene (15 c.c.) were kept at room temperature for 1 hr., then for 5 min. on the water-bath. Stannic chloride (0·4 c.c.) in benzene (0·4 c.c.) was added to the solution at 0° and the mixture left for 15 min. The complex was decomposed with ice and hydrochloric acid, and the benzene solution separated. The *ketone* (0·33 g.), recovered in the usual manner and crystallised from *cyclo*hexane, had m. p. 163—164° (Found : C, 85·8; H, 7·9. $C_{17}H_{18}O$ requires C, 85·7; H, 7·6%). Light absorption : max. 222 (infl. 255—260), 330—340 mμ [log ε 4·70 (4·17), 3·83].

2 : 3 : 9-*Trimethylphenanthrene*. The foregoing ketone (0·15 g.) was reduced with lithium aluminium hydride (0·24 g.) in boiling ether for 3 hr. The *alcohol*, isolated in the usual manner and crystallised from benzene, had m. p. 175—177° (Found : C, 85·2; H, 8·5. $C_{17}H_{20}O$ requires C, 84·95; H, 8·4%).

The alcohol (0·15 g.) was dehydrated with fused potassium hydrogen sulphate (0·015 g.) at 180° for 10 min. and the distilled product was dehydrogenated in carbon dioxide with 30% palladium–charcoal (0·1 g.) at 240°. 2 : 3 : 9-*Trimethylphenanthrene* was sublimed from the mixture and crystallised from methanol as plates, m. p. 107—108° (Found : C, 92·9; H, 7·2. $C_{17}H_{16}$ requires C, 92·7; H, 7·3%). Light absorption : max. 255, 272, 280, 300, 320, 328, 334, 352 mμ (log ε 4·84, 4·32, 4·23, 4·02, 2·61, 2·53, 2·64, 2·67). The *picrate* formed orange-red needles (from ethanol), m. p. 179—181° (Found : C, 61·2; H, 4·3. $C_{17}H_{16},C_6H_3O_7N_3$ requires C, 61·5; H, 4·3%).

γ-(3 : 6 : 7-*Trimethyl*-1-*naphthyl*)*butyric acid*. This *acid* was obtained in 90% yield from β-(3 : 6 : 7-trimethyl-1-naphthoyl)propionic acid as described above for the 2-naphthylbutyric acid. It had m. p. 155—159° (from benzene) (Found : C, 80·0; H, 8·0%).

1 : 2 : 3 : 4-*Tetrahydro*-6 : 7 : 10-*trimethyl*-1-*oxophenanthrene*. The above butyric acid (0·9 g.) was converted into its acid chloride with phosphorus pentachloride (1 g.) in benzene, and this was cyclised with stannic chloride (1 c.c.) as described above. The *ketone* (0·9 g.) crystallised from benzene–light petroleum as prisms, m. p. 129—130° (Found : C, 85·6; H, 7·9%). Light absorption : max. 260, 294, 304, 356 mμ (log ε 4·96, 4·22, 4·17, 3·48).

2 : 3 : 8 : 9-*Tetramethylphenanthrene*. The foregoing ketone (0·9 g.) in benzene was added to ethereal methylmagnesium iodide [from methyl iodide (6 g.) and magnesium turnings (1 g.)]. Most of the ether was distilled off and the mixture refluxed in benzene solution for 3 hr. The crude product was isolated in the usual way, and was dehydrated and dehydrogenated simultaneously by 30% palladium–charcoal (0·1 g.) at 280—290° in carbon dioxide. After chromatography on alumina with light petroleum (b. p. 60—80°), 2 : 3 : 8 : 9-*tetramethylphenanthrene* was obtained as colourless plates m. p. 106—107° (from methanol) (Found : C, 92·6; H, 7·7. $C_{18}H_{18}$ requires C, 92·3; H, 7·7%). Light absorptions : max. 260, 282, 293, 305, 324, 339·5, 356 mμ (log ε 4·81, 4·15, 4·03, 4·09, 2·89, 3·07, 3·08). The *picrate* formed orange-red needles (from ethanol), m. p. 167—169° (Found : C, 62·5; H, 4·8. $C_{18}H_{18},C_6H_3O_7N_3$ requires C, 62·2; H, 4·6%), and the *s*-trinitrobenzene *complex* yellow needles, m. p. 181—183° (Found : C, 64·7; H, 4·7. $C_{18}H_{18},C_6H_3O_6N_3$ requires C, 64·4; H, 4·8%).

One of us (W. C.) was supported by the Medical Research Council. We are indebted to the Department of Scientific and Industrial Research for a maintenance allowance (to J. D. G.). Microanalyses were by Mr. J. M. L. Cameron and Miss M. Christie.

UNIVERSITY OF GLASGOW. [*Received, December 14th*, 1956.]

470. *The Configuration of the So-called "Diphenylmaleinitrile."*

By A. J. Williams and R. J. W. Le Fèvre.

Cook and Linstead [1] found "diphenylmaleinitrile" a suitable starting material for the preparation of porphyrazines. A *cis*-configuration was accepted because of the ease of conversion into a cyclic imide or, through the acid, into the corresponding anhydride. Linstead and Timmons [2] raised the possibility that the dinitrile was the *trans*-, and not the *cis*-form, as had previously been supposed. Very recently Timmons and Wallwork [3] reported that *X*-ray analysis indicates a *trans*-structure of the molecules in the crystal.

The problem seemed one in which polarity measurements should be helpful. Specimens of "diphenylmaleinitrile" were prepared as described by Cook and Linstead [1] and purified chromatographically in benzene over alumina; after crystallisation from benzene–light petroleum the material appeared as white needles, m. p. 161° (lit.,[4] various between 156° and 160°).

Dielectric-constant and density observations were made on solutions in carbon tetrachloride by means of the apparatus noted in ref. 5. Symbols and procedures have been explained before.[6] At first considerable irregularities were found when ϵ_{12} values were plotted against concentration; later these were traced to the fact that daylight rapidly caused the dielectric constant of a solution to increase. The Table lists the results obtained before and after about 4 hours' exposure, in ordinary glass flasks, to bright sunlight.

Dielectric polarisation measurements of "diphenylmaleinitrile," m. p. 161°.

Before illumination

$10^5 w_2$	168·5	193·7	250·3	255·0	281·4	313·8	336·8	344·8	364·8
ϵ^{25}	2·2290	2·2295	2·2298	2·2321	2·2339	2·2291	2·2336	2·2362	2·2346
d_4^{25}	—	1·5833	—	1·5830	1·5828	1·5828	1·5825	1·5824	1·5823

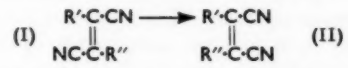
After illumination

$10^5 w_2$	241·3	255·0 *	281·4	344·8	364·8
ϵ^{25}	2·3006	2·3055	2·2891	2·3277	2·3303
d_4^{25}	—	1·5830	—	$1·5825_5$	$1·5824_5$

* This solution was illuminated for 6 hr., *i.e.*, 1·5 times as long as were the other three.

	$(\alpha\epsilon_1)_{mean}$	$(\beta d_1)_{mean}$	$_\infty P_2$ c.c.	$_DP$ (c.c.)	μ (D)
Before illumination	1·79	$-0·606_6$	102·0	78·5	$1·0_7$
After illumination	28·1	$-0·377_8$	737·8		$5·6_8$

In order to compute the apparent dipole moments an estimate of the distortion polarisations has been made from the $_TP$ (29·7 c.c.) reported by Bloom and Sutton [7] for fumaronitrile in benzene, together with the group refractions for H (1·03 c.c.) and C_6H_5 (25·36 c.c.)



given by Vogel.[8] Relevant data are at the foot of the Table. The moments emerge as 1·1 D and 5·7 D. Such a marked difference can be most obviously explained by light effecting the change (I) ⟶ (II). The preparation having m. p. 161° is therefore recognised as

[1] Cook and Linstead, *J.*, 1937, 929.
[2] Linstead and Timmons, quoted by Linstead, *J.*, 1953, 2873.
[3] Timmons and Wallwork, *Chem. and Ind.*, 1955, 62.
[4] Beilstein's *Handbuch*, 4th edn., 1926, IX, 945, also second supplement, IX, 675.
[5] Buckingham, Chau, Freeman, Le Fèvre, Narayana Rao, and Tardif, *J.*, 1956, 1405.
[6] Le Fèvre, "Dipole Moments," Methuen, London, 3rd edn., 1953, Chap. 2.
[7] Bloom and Sutton, *J.*, 1941, 727.
[8] Vogel, *J.*, 1948, 1833.

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predominately of *trans*-content. That the observed moment is not nearer to zero may be due to at least two causes : an underestimation of ${}_{D}P$, and the sensitivities of the solutions to light. We note that, during our work, the isomerides (I) and (II) with R″ = H have been reported to have moments of 1·9 and 6·1 D (" preliminary values ") by Beech and Piggott,[9] or 2·71 and 7·98 D by Schneider.[10] The polarity differences are roughly of the same order as those shown in the Table for $(CN{\cdot}CPh{:})_2$; however, in neither case is photoisomerisation mentioned.

The material of m. p. 161° has also been examined, with exclusion of daylight, as 10^{-4}M- and 5×10^{-4}M-solutions in ethanol, in a Hilger " Uvispek " spectrophotometer. Three maxima of ultraviolet absorption were noted : at 237·5 mμ (log ε 4·22), at 263 mμ (log ε 3·98), and *ca.* 339 mμ (broad ; log ε 4·37). Exposure to bright sunlight for 15 min. caused marked alterations : the intensity of the first band was slightly weakened (to log ε 4·08), that of the second band was raised (to log ε 4·33), and that of the third band diminished (to log ε *ca.* 3·6). Only at 237·5 mμ was no wavelength shift noted ; illumination moved the 263·0 mμ maximum to 267·2 mμ, and destroyed the broad smooth peak centred around 339 mμ, producing in its place signs of maxima of lower intensity between 320 and 350 mμ together with two peaks at 374·2 mμ (log ε 2·98) and 399·5 mμ (log ε 2·94). Both in the dielectric constant and in the photometric measurements no reversion to the pre-illumination state was observed after prolonged storage in the dark. The diminution of intensity of the band at *ca.* 339 mμ, produced by irradiation, is reminiscent of the behaviour of the *K*-bands of many azo-derivatives, when similarly treated (cf. refs quoted by Le Fèvre and Sousa [11]), and is in harmony with the spectra of *trans*- and *cis*-stilbene,[12] *syn*- and *anti*-oximes,[13, 14] etc.

Present observations therefore support the conclusions of refs. 2 and 3. Presumably the isomeride with m. p. 243° (quoted in ref. 4) is in fact diphenylmaleinitrile(*cis*), and the configurations hitherto written for the two isomers of $(CN{\cdot}CPh{:})_2$ should be interchanged. This pair, and the αβ-dicyanostyrenes already mentioned, thus seem to be uncommon cases among geometrical isomerides in that the higher-melting form is the *cis*- and not the *trans*-form.

Grateful acknowledgments are made to Beetle-Elliott Ltd. for a scholarship to A. J. Williams.

UNIVERSITY OF SYDNEY, N.S.W., AUSTRALIA. [*Received, December 27th*, 1956.]

[9] Beech and Piggott, *J.*, 1955, 423.
[10] Schneider, *J. Amer. Chem. Soc.*, 1955, **77**, 2796.
[11] Le Fèvre and Sousa, *J.*, 1955, 3154; 1957, 745.
[12] Smakula and Wassermann, *Z. phys. Chem.*, 1931, *A*, **155**, 353.
[13] Brady, *J.*, 1914, **105**, 2104; Brady and Grayson, *J.*, 1933, 1037.
[14] Raffouf, *J. Amer. Chem. Soc.*, 1946, **68**, 1765.

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471. *The Effect of Potassium Iodide Concentration on the Oxidation of Glucose by Alkaline Iodine Solutions.*

By R. L. Colbran and T. P. Nevell.

During an investigation of the oxidation of the reducing end-groups in hydrocelluloses by alkaline solutions of iodine, it was found that the reaction was considerably affected by the concentration of potassium iodide in the reagent. It is well known that the hypoiodite in these solutions disproportionates to iodate and iodide, and it has several times been reported [1] that, in solutions of moderate alkalinity, this reaction is retarded by increasing the total iodide concentration. We have found no mention of the effect of this on the oxidation of aldoses, however, and some experiments were therefore made to show the effect of iodide concentration on the oxidation of glucose.

The work was done at 20° with 0·01N-iodine in a carbonate–bicarbonate buffer of pH 10·8. Fig. 1 shows the effect of potassium iodide concentration on the rate at which the concentration of available iodine (*i.e.*, free hypoiodous acid, hypoiodite ion, tri-iodide ion, and free iodine) falls under these conditions as a result of disproportionation. The results were obtained by adding an excess of 0·02N-sodium arsenite to aliquot portions of the solution, and back-titration with 0·01N-iodine, the arsenite being buffered so that the pH of the mixture was 6·7. Whereas with 8 g. of potassium iodide per l. nearly all the iodine has been converted into iodate and iodide within 5 hr., with 80 g. per l. a substantial proportion of the iodine remains available for oxidation purposes even after two days. According to Ingles and Israel,[2] the oxidising species in alkaline solutions of iodine is hypoiodous acid. In the solutions mentioned above, however, only a small proportion of the available iodine is present as hypoiodous acid; the rest exists largely as tri-iodide ion. If the hydrolysis constant of iodine K_1, the dissociation constant of hypoiodous acid K_2, and the equilibrium constant for the formation of tri-iodide ion K_3, are known, the concentration of undissociated hypoiodous acid present at any time in a given solution can be calculated from the curves in Fig. 1. Specimen results of these calculations are given in the Table. The following values for the constants were used: $K_1 = 1{\cdot}56 \times 10^{-13}$ at 20° (calc. from values [3] at 0° and 25°), $K_2 = 4{\cdot}5 \times 10^{-13}$ (Skrabal [4]), $K_3 = 806$ at 20° (calc. from values [5] at 0° and 25°).

	[HOI] (10^{-7}M)			
Time of decomp. (hr.)	0	4	10	24
KI present : 8 g./l.	3·12	3·32	2·24	1·02
80 g./l.	2·67	2·48	2·24	1·95

Fig. 1 and the Table show that, in a solution containing 8 g. of potassium iodide per l., the concentrations of hypoiodous acid and of available iodine fall rapidly to low values. In a solution containing 80 g. of potassium iodide per l., however, the hypoiodous acid concentration is always very low, but it remains nearly constant, and the concentration of available iodine remains high.

The rate of oxidation of D-glucose (0·00111M) by 0·01N-iodine at pH 10·8 and 20° was measured by adding acid to aliquot portions of the reaction mixture after various times, and titrating the liberated iodine with thiosulphate. The results for solutions containing

[1] Lonnes, *Z. anal. Chem.*, 1894, **33**, 409; Forster, *J. phys. Chem.*, 1903, **7**, 640; Skrabal, *Monatsh.*, 1911, **32**, 815.
[2] Ingles and Israel, *J.*, 1948, 810.
[3] Jones and Hartmann, *J. Amer. Chem. Soc.*, 1911, **33**, 1485; Bray and Connolly, *ibid.*, 1915, **37**, 241.
[4] Skrabal, *Ber.*, 1942, **75**, 1570.
[5] Jones and Kaplan, *J. Amer. Chem. Soc.*, 1928, **50**, 1845.

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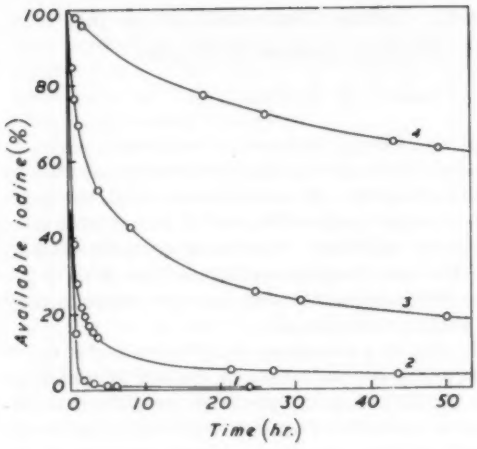

FIG. 1. *Effect of potassium iodide concentration on the stability of* 0·01N-*iodine at* pH 10·8 *and* 20°.

KI per l. : (1) 8 g., (2) 20 g., (3) 40 g., (4) 80 g.

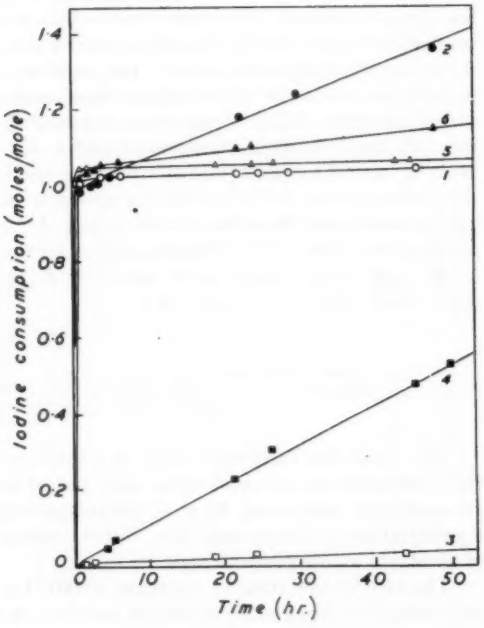

FIG. 2. *Effect of potassium iodide concentration on the rate of oxidation of* 0·00111M-D-*glucose,* -D-*glucono-γ-lactone, and* -D-*glucuronolactone by* 0·01N-*iodine at* pH 10·8 *and* 20°.

(1, 2) Glucose; (3, 4) gluconolactone; (5, 6) glucuronolactone. (1, 3, 5) 8 g. of KI per l. (2, 4, 6) 80 g. of KI per l.

8 g., and 80 g., of potassium iodide per l. (see Fig. 2) show that a consumption of 1 mole of iodine per mole of glucose (corresponding to the formation of gluconic acid) was attained within 2 hr. in both reagents. This consumption was, however, reached more quickly in the presence of 8 g., than of 80 g., of potassium iodide per l., as would be expected from the figures in the Table. It may also be seen from Fig. 2 that, whilst in the first solution oxidation had virtually ceased when the amount of iodine reduced was equivalent to the conversion of the glucose into gluconic acid, in the second solution further oxidation (" over-oxidation ") occurred at a low, but constant, rate. Similarly, D-glucono-γ-lactone (0·00111M) was hardly oxidised at all by the reagent containing 8 g. of potassium iodide per l., but was oxidised at a constant rate by that containing 80 g. per l. (Fig. 2). It thus appears that the oxidation of groups other than semiacetal groups cannot be due to hypoiodous acid, since the concentration of this species is higher in the first solution than in the second at all times up to 10 hr.

The oxidation of D-glucuronolactone (0·00111M) was also examined in the presence of 8 g. and 80 g. of potassium iodide per l.; the results are shown in Fig. 2. The rate curve is almost identical with that for glucose in the first solution, but the rate of over-oxidation is much lower than that of glucose in the second solution. This suggests that the over-oxidation of glucose is mainly a reaction of the primary, rather than the secondary, alcohol groups.

The divergence of opinion on the extent to which over-oxidation interferes with the determination of aldoses by the iodine method may be due to the use of different concentrations of potassium iodide by various workers. The results presented here demonstrate the importance of keeping this concentration as low as possible, consistent with the necessity of maintaining a sufficient excess of available iodine until the oxidation is complete.

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472. *The Heat of Formation of Cyanuric Chloride and the Heat of Trimerisation of Cyanogen Chloride.*

By A. R. HUMPHRIES and G. R. NICHOLSON.

THE only published value for the heat of formation of cyanuric chloride, −107·9 kcal./mole, was calculated by Lemoult [1] from his value of the heat of combustion of the solid compound, 292·9 kcal./mole. Lemoult did not state what the products of combustion were, but if we assume that all of the chlorine went to Cl_2(g) the heat of formation of cyanuric chloride should be +10·7 kcal./mole, and if, alternatively, we assume that sufficient water was present, and fairly dilute hydrochloric acid with no Cl_2(g) was formed, the derived heat of formation should be about −4 kcal./mole. The origin of the value −107·9 kcal./mole is obscure. We therefore redetermined the heat of formation of cyanuric chloride and incidentally obtained a value for the heat of trimerisation of cyanogen chloride.

Experimental.—A suitable calorimetric bomb was not available for determining the heat of combustion of chlorine-containing compounds, so the heat of hydrolysis of cyanuric chloride to cyanuric acid was measured. The calorimeter was a Bunsen-type naphthalene calorimeter described by Beynon and Humphries; [2] this operates isothermally at the m. p. of naphthalene. Hydrolysis was complete in 1½ hr. at 80° in a buffer solution composed of 2·5 moles each of acetic

[1] Lemoult, *Compt. rend.*, 1896, **123**, 1276.
[2] Beynon and Humphries, *Trans. Faraday Soc.*, 1955, **51**, 1065.

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acid and sodium acetate made up to 1 l. with distilled water. Completeness of the reaction was checked by titration of the final solution for chloride ion.

The buffer solution (20 c.c.) was placed in the reaction chamber of the calorimeter, a sealed glass capsule containing a weighed amount (about 0·2 g.) of cyanuric chloride was lowered into it and held submerged by the stirrer, and hydrolysis was started by shattering the capsule with the stirrer. The solution was thereafter stirred at regular intervals until reaction was complete. The heat evolved was measured by observing the movement of a mercury thread forced along a calibrated capillary tube by the melting of some of the naphthalene mantle around the reaction chamber. The reaction could be represented as :

$$y(CNCl)_3(s) + 3yH_2O(sol.) \longrightarrow y(CNOH)_3(sol.) + 3yHCl(sol.),$$

in which y was the molar quantity of cyanuric chloride used, the $3y$ moles of water were from the buffer solution, and the y moles of cyanuric acid and $3y$ moles of hydrochloric acid formed were in solution in the buffer from which $3y$ moles of water had been removed. The latter solution was referred to as solution 1. If Δh was the heat of the above reaction, then :

$$\Delta h = \Delta H_f[y(CNOH)_3 \text{ in solution 1}] + \Delta H_f[3yHCl \text{ in solution 1}] - \Delta H_f[y(CNCl)_3(s)] - \Delta H_f[3yH_2O \text{ in buffer}] \quad . \quad . \quad . \quad . \quad . \quad (1)$$

In order to determine the heat of formation of cyanuric chloride it was therefore necessary to know the other three heats of formation appearing in equation (1).

$\Delta H_f[y(CNOH)_3$ in solution 1] was obtained by measuring the heat of solution of y moles of cyanuric acid in a solution consisting of 20 c.c. of buffer plus $3y$ moles of hydrochloric acid, and making use of a known value for the heat of formation of solid cyanuric acid. $\Delta H_f[3yHCl$ in solution 1] was obtained by measuring the heat of solution of $3y$ moles of a known aqueous solution of hydrochloric acid in 20 c.c. of buffer in which y moles of cyanuric acid had been dissolved. A correction was then made for the heat of dilution of solution 1 by an amount of water corresponding to that present in the aqueous hydrochloric acid used. $\Delta H_f[3yH_2O$ in buffer] was similarly determined by measuring the heat of dilution by water of the buffer solution. Each of the above three auxiliary quantities was measured in the naphthalene calorimeter.

The results obtained were :

(i) Two measurements of Δh gave −95·44 and −95·33 kcal./mole; mean −95·39 kcal./mole of solid cyanuric chloride.

(ii) Three measurements of the heat of solution of cyanuric acid as above gave +5·95, +5·82, and +5·94 kcal./mole; mean +5·90 kcal./mole of solid cyanuric acid. This was taken in conjunction with a value [3] for the heat of combustion of solid cyanuric acid, 219·5 kcal./mole, which is equivalent to a heat of formation of −165·1 kcal./mole, to give $\Delta H_f[(CNOH)_3$ in solution 1] = −159·2 kcal./mole.

(iii) Measurements of the heat of solution of two widely different concentrations of aqueous hydrochloric acid (HCl,xH_2O with x approx. 23·2 and 3·6) as above, gave, after corrections for the heat of dilution of solution 1 by the corresponding quantities of water, −39·35 and −40·18 kcal./mole; mean −39·76 kcal./mole of hydrochloric acid for ΔH_f[HCl in solution 1]. Values for the heats of formation of HCl,xH_2O, which were required in the calculation, were obtained from the literature.[4]

(iv) The heat of dilution of the buffer solution by water was very small, and this measurement led to $\Delta H_f[H_2O$ in buffer] = −68·33 kcal./mole of water, the value [4] −68·32 kcal./mole for the heat of formation of water (liquid) being used.

The results (i)—(iv) were combined by means of equation (1) to give :

$$-95·39 = -159·2 + 3(-39·76) - \Delta H_f[(CNCl)_3(s)] - 3(-68·33)$$

giving +21·9 kcal./mole for the heat of formation of solid cyanuric chloride. The measured values used in obtaining this result were all applicable to 80°, whereas the published data used

[3] Thermochemical Bull., March 1955, p. 2. (International Union of Pure and Applied Chemistry. Sub-Commission on Experimental Thermochemistry.)

[4] "Selected Values of Chemical Thermodynamic Properties," U.S. Dept. Commerce, Nat. Bur. Standards, Washington, D.C., 1949.

were applicable to 25°. It was estimated that the net correction to the final result to give its value at 25° would be small compared with the overall experimental error (considered to be ± 1 kcal./mole in view of the indirect nature of the determination).

This result was combined with the heat of formation of cyanogen chloride (gas) given by Lord and Woolf [5] (+31·6 kcal./mole) to obtain the value −72·9 kcal. for the heat of trimerisation at 25°, $3CNCl(g) \longrightarrow (CNCl)_3(s)$. It is interesting that Lemoult [1] gave the value −189·05 kcal. for the heat of the trimerisation, $3CNCl(l) \longrightarrow (CNCl)_3(s)$, based on his erroneous value for the heat of formation of cyanuric chloride and a value by Berthelot (+27·05 kcal./mole) for the heat of formation of cyanogen chloride (liquid).

The authors thank Dr. D. J. Berets of the American Cyanamid Company for permission to use his value of the heat of combustion of cyanuric acid which has not yet been formally published.

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[5] Lord and Woolf, *J.*, 1954, 2546.

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473. *The Heat of Combustion of Acetylacetone.*

By G. R. NICHOLSON.

THE heat of combustion of acetylacetone (liquid) was required in connection with a thermochemical calculation. The only measured value in the literature appeared to be that by Guinchant [1] in 1895 (615·9 kcal./mole). Kharasch,[2] in his well-known compilation of heats of combustion, considered Guinchant's value to be too low and gave an alternative value (638·2 kcal./mole) calculated by his own method involving the structural formula of the compound. In view of this uncertainty it was thought advisable to make a new determination.

Experimental.—An isothermal bomb calorimeter of Dickinson type [3] was used, the calorimeter having previously been calibrated by combustion of benzoic acid (Nat. Bur. Standards sample No. 39 g). Calorimeter temperatures were measured with a platinum resistance thermometer of Meyers's [4] type, which had been constructed and calibrated at fixed points in this laboratory, in conjunction with a Smith's difference bridge. Soda-glass ampoules were completely filled with acetylacetone by means of a hypodermic syringe, and then sealed. Filled ampoules were pressure tested at 30 atm. (equal to the initial oxygen pressure in the bomb), and those surviving were used for combustion. The weight of liquid used, which depended on the size of the individual ampoule, was 1·3—2·0 g. To assist bursting, the ampoules were smeared locally with about 0·01 g. of petroleum jelly which was ignited by means of a platinum wire and cotton-thread fuse. Corrections to the gross heat evolved were made for the heats of combustion of the cotton and petroleum jelly (previously determined), the joule heat in the platinum wire, and the heat produced in the formation of a small quantity of nitric acid in the bomb from residual nitrogen in the oxygen. Corrections were also made for small quantities of residual carbon (0·1—0·8 mg.) found fused in the remains of the ampoule after combustion. Sample weights were corrected for buoyancy by using a density [5] of 0·976 g./c.c. for acetylacetone.

Two fractions of acetylacetone were used, severally of b. p. 71—72°/101—101·5 mm., b. p. 71·5—72°/101·5 mm. Three combustions on fraction 1 gave a mean $-\Delta H_c^\circ/M = 6{\cdot}4944 \pm 0{\cdot}0036$ kcal./g., and five combustions on fraction 2 gave $-\Delta H_c^\circ/M = 6{\cdot}4693 \pm 0{\cdot}0022$ kcal./g. These results referred to the usual standard conditions (isothermal combustion of the liquid at 25°

[1] Guinchant, *Compt. rend.*, 1895, **121**, 354.
[2] Kharasch, *Bur. Stand. J. Res.*, 1929, **2**, 359.
[3] Dickinson, *Bull. Bur. Stand.*, 1915, **11**, 189.
[4] Meyers, *Bur. Stand. J. Res.*, 1932, **9**, 807.
[5] "Handbook of Chemistry and Physics," Chemical Rubber Publ. Co., Cleveland, Ohio, 37th Edn., 1955.

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and a constant pressure of 1 atm.), with CO_2(g) and H_2O(l) as products of combustion, and the estimated error was calculated by combining the combustion error (twice the standard error of the mean $-\Delta H_c^\circ/M$) and the benzoic acid calibration error.

In order to see if impurities in these fractions could be identified, both were examined in a mass spectrometer. It was found that the impurity consisted almost entirely of xylene in each case, and it was estimated that fraction 1 contained 2·08% by weight of xylene and fraction 2 1·42%. It was not possible to distinguish amongst the three isomers of xylene, but, fortunately, their heats of combustion are very nearly identical [6] (1088·16 kcal./mole for the *ortho*- and *para*-forms, and 1087·92 kcal./mole for the *meta*-form). It was assumed that the impurity consisted entirely of xylene with $-\Delta H_c^\circ = 1088{\cdot}16$ kcal./mole, or $-\Delta H_c^\circ/M = 10{\cdot}2502$ kcal./g. Calculation then showed that, for acetylacetone alone, fraction 1 gave $-\Delta H_c^\circ/M = 6{\cdot}4146$ kcal./g. and fraction 2 gave 6·4148 kcal./g. These two values were in very satisfactory agreement, and the mean, $-\Delta H_c^\circ/M = 6{\cdot}4147$ kcal./g., is equivalent to $-\Delta H_c^\circ = 642{\cdot}20$ kcal./mole, 100·114 being used as the molecular weight. The estimated error may be taken as $\pm 0{\cdot}36$ kcal./mole.

This result is much higher than Guinchant's value, but is only about 0·6% higher than Kharasch's calculated value

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[6] "Selected Values of Properties of Hydrocarbons," U.S. Dept. Commerce, Nat. Bur. Standards, Washington, D.C., 1947.